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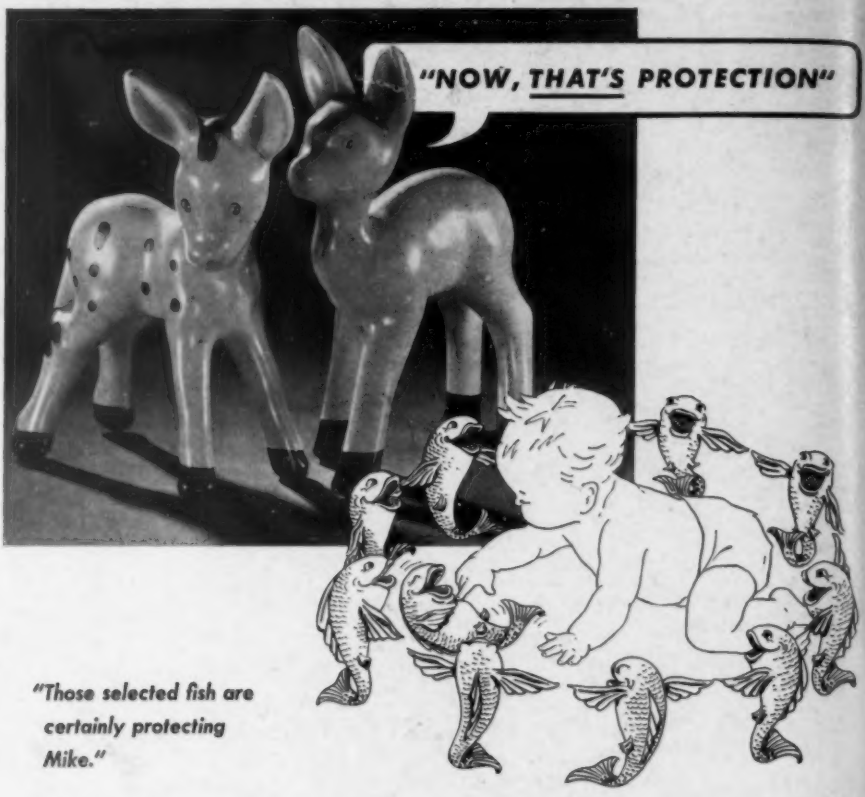
TABLE OF CONTENTS ON 3rd COVER



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Original Communications

THE MECHANISM OF MUSCLE SPASM IN POLIOMYELITIS

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CLINICAL DESCRIPTION OF MUSCLE SPASM

ONE of the fundamental innovations of the Kenny concept of poliomyelitis[1, 2] is the emphasis placed upon "muscle spasm." This is a condition characterized by shortening of the skeletal muscles which appears in the acute stage of the disease and may persist for months or years. It may be identified in the early stages by characteristic deformities, by prominence of tendons, by flatness and narrowing of muscle bellies, by increase or decrease in the number and depth of skin folds or creases, by limitation of range of passive joint motion, and by other evidences of muscle shortening. The muscles in spasm are painful to stretch or pressure and may often be weak or even completely paralyzed. Spasm may be the direct cause of loss of function in opposing muscles because of the mechanical interference with motion produced by the shortened painful muscle. Relief of this condition may lead to increased active as well as passive motion and increased power in apparently paralyzed muscles by removal of this mechanical obstruction. Failure to relieve "spasm" by energetic and persistent therapy may result in permanent deformity as well as dysfunction of antagonistic and synergistic muscles.

This phenomenon, which is apparently present in every case of poliomyelitis, is essentially an abnormally increased tonus of the skeletal muscles. It is not, however, a relative increase in tonus due to weakness of opposing muscles as is commonly thought. Clinical observations have shown that there is no constant relationship between spasm and paralysis caused by motor denervation. Examples have been seen where "spasm" is present in extremities in which all active motor power has been lost in all muscles, both those that are shortened and those that are lengthened. Other cases show severe spasm in muscles whose opponents retain normal power.

From the University of Minnesota.

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Two types of "muscle spasm" may be identified.

1. *Muscle hypertonus.* This is a markedly increased muscle tonus which may persist without relaxation for months or years. Hypertonus not only causes limitation of joint motion, but also frequently causes gross deformities. In the gastrocnemius-soleus group it causes so-called "foot drop," more accurately named "foot retraction." In the upper trapezius, it causes an elevated shoulder which may, in turn, be the cause of a scoliosis. In one quadratus lumborum it results in a unilateral lordosis with pelvic tilt and apparent leg shortening. Lordosis or scoliosis may result from hypertonus in the muscles of the back.

2. *Hyperirritable stretch reflex.* In this type, there is a limitation of the range of passive motion which is variable in degree. There is no resistance to passive stretch of the involved muscle until the point of limitation of motion is approached, when further passive motion becomes impossible due to the resistance of the strongly contracted, painful muscle. A slight decrease in stretch of the muscle, produced by a return of a few degrees toward the resting position, relieves the pain and terminates the strong contraction of the muscle. This appears to be a stretch reflex, whose "trigger mechanism" is set at a much lower level than normal. Since there is no resistance to passive stretch through a certain range of motion, this phenomenon differs from the rigidity in Parkinson's disease and the spasticity in hemiplegia.

Hyperirritable stretch reflexes are observed in poliomyelitis most commonly in the hamstring, quadriceps, adductor, pectoralis major, and latissimus dorsi muscles. It may also occur in the triceps brachii, wrist flexors, and other muscles.

Muscle hypertonus and hyperirritable stretch reflex are closely related and may have the same fundamental mechanism. They both appear to be dependent upon hyperirritability of the spinal mechanism for proprioceptive reflexes and muscle tonus.

The distribution of muscle spasm varies in different cases and may not be symmetrical bilaterally. It may be localized in a single muscle or group of muscles in a limb. It may involve both agonist and antagonist muscles about a particular joint. Many of the milder cases of poliomyelitis show muscle spasm but no permanent paralysis or atrophy. On the other hand, spasm may be severe in muscles which remain paralyzed and undergo atrophy.

In a particular muscle, the spasm has a number of characteristic clinical features:

1. There is limitation of the range of passive motion, variable in degree, but usually marked. This is observed in both "hypertonus" and "hyperirritable stretch reflex."

2. The muscle is painful to stretch or pressure. While spontaneous pain usually disappears following the acute stage of the disease, the tenderness to stretch is present as long as the muscle spasm persists, frequently for many months.

3. The shortening of the muscle in the acute stage may be increased by attempts at forced motion, rough handling, electrical stimulation, or anything that increases pain.

4. Muscle spasm may be remarkably persistent. Untreated muscle spasm often persists for months or years. Even with active therapy beginning in the acute stage, spasm may not be relieved for many months. On the other hand, in milder cases, spasm may subside spontaneously.

5. Deformity frequently results from marked hypertonus. Examples are as follows: "foot retraction" from spasm in the posterior calf muscles, elevated shoulder from spasm in the upper trapezius, apparent leg shortening from spasm in the quadratus lumborum muscle.

6. If the spasm persists for a long period of time, irreversible contracture may result.

7. The muscle in spasm is often weak and sometimes paralyzed. Voluntary contraction of the muscle may be decreased or absent. This is an interesting paradox: a muscle strongly contracted in tonus and proprioceptive reflexes which is weak or incapable of voluntary contraction.

8. Many muscles in spasm do not undergo permanent atrophy and recover function completely with therapy. Muscles in spasm may, however, even after relief of the spasm, remain paralyzed and undergo marked atrophy.

9. Spontaneous fasciculation is not characteristic of muscles in spasm.

THE NEUROGENIC BASIS OF MUSCLE SPASM

In an attempt to determine the mechanism of muscle spasm in clinical cases of poliomyelitis, we carried out a number of experiments on patients at various periods after the onset of this disease.* Five patients were subjected to intravenous pentothal anesthesia in order to produce loss of consciousness and elimination of pain. Muscle spasm in various muscle groups was determined quantitatively by measuring the angle of limitation of motion with a goniometer (Table I). In some patients, no significant change was noted. In other patients, a slight to moderate decrease in limitation of motion was observed. In no instance, however, was there complete relaxation of the muscle spasm under pentothal anesthesia. These results suggest that pain may be a factor tending to increase muscle spasm in some instances, but that it is not of primary importance in its mechanism.

In five patients, spinal anesthesia was performed with injection of from 100 to 150 mg. of procaine intrathecally. In acute and subacute cases, spinal anesthesia led to relaxation of muscle spasm to a marked extent (Table I). On the other hand, in two patients, fourteen months

*These experiments were carried out with the cooperation of Dr. Scott M. Smith, Dr. N. Sonnesyn, and Dr. R. T. Knight of the Department of Anaesthesia, University of Minnesota Hospitals. Their assistance and cooperation are gratefully acknowledged.

TABLE I

EFFECT OF ANESTHESIA ON MUSCLE SPASM IN POLIOMYELITIS

	CASE	TIME SINCE ONSET	TYPE OF ANESTHESIA	HAMSTRING		GASTROCNEMIUS-SOLEUS GROUP		SOLEUS		QUADRICEPS		ABDUCTION (LEGS)
				R	L	R	L	R	L	R	L	BOTH LEGS
Before	1	2½ mo.	P	50	55	100	105					55
During	1	2½ mo.	P	60	60	100	105					60
Before	1	2½ mo.	S	45	50	100	105	95	90	75	75	60
During	1	2½ mo.	S	75	70	95	95	90	95	60	60	70
Before	2	1 mo.	P	30	30	115	120	110	115	85	85	35
During	2	1 mo.	P	55	50	115	120	110	115	50	45	55
Before	2	1 mo.	S	30	25	125	130	115	120	80	85	35
During	2	1 mo.	S	70	75	100	105	95	95	*	*	70
Before	3	2 mo.	P	35	40	105	100	100	90	45	40	55
During	3	2 mo.	P	65	55	105	100	95	90	*	*	65
Before	3	2 mo.	S	45	40	110	105	100	95	55	50	45
During	3	2 mo.	S	80	80	100	95	95	95	*	*	70
												R L
Before	4	3 wk.	P	40	40	105	100	85	80	90	90	35 45
During	4	3 wk.	P	45	50	105	105	95	85	75	80	35 40
Before	5	2 mo.	P	35	35	115	115					25 25
During	5	2 mo.	P	30	30	105	110					25 25
												BOTH LEGS
Before	6	14 mo.	S	60	50	100	95	100	95	120	120	45
During	6	14 mo.	S	60	60	100	95	95	95	115	120	50
Before	7	14 mo.	S	55	55	120	115	105	115	90	75	60
During	7	14 mo.	S	55	55	115	110	110	95	80	70	65

*Heel touches buttock.
P = Pentothal anesthesia.
S = Spinal anesthesia.

TABLE II

PROGRESSIVE DECREASE IN MUSCLE SPASM WITH MORE COMPLETE BLOCK OF MOTOR NERVE ROOTS FOLLOWING INTRATHECAL ADMINISTRATION OF PROCAINE

PATIENT E. F. AGE, 12 YR. TIME SINCE ONSET, 2 MO.	TIME	SENSORY LEVEL	HAMSTRING		GASTROCNEMIUS-SOLEUS GROUP		QUADRICEPS		ABDUCTION BOTH LEGS
			R	L	R	L	R	L	
Before anesthesia	3:55		45	40	110	105	55	55	45
Intrathecal procaine 100 mg.	4:05								
Sensory anesthesia	4:12	T 10	60	60	100	100	*	*	65
Motor block	4:20	T 4	70	70	105	100	*	*	70
Motor block	4:32		80	80	100	95	*	*	70
Beginning recovery	4:44		70	75	105	105	*	*	70

*Heel touches buttock.

after the onset of the disease, spinal anesthesia produced practically no change in the limitation of passive motion (Table I). At our suggestion, Dr. Malcolm Cook, Department of Pediatrics, Washington University, St. Louis, carried out spinal anesthesia on two patients with acute poliomyelitis within two weeks after the onset of the disease and observed elimination of muscle spasm.

In two patients, measurements were made of limitation of passive motion at various periods after introduction of procaine into the spinal canal. With complete sensory anesthesia but incomplete block of the motor nerve roots, the relaxation of muscle spasm was not as great as was observed later with complete motor block (Table II).

In one patient, beta-erythroidine hydrochloride was injected intravenously eight and one-half months after onset of poliomyelitis. Marked relaxation of muscle spasm and of pain on passive motion was observed at the height of the drug effect. This drug has a curare-like action in blocking the myoneural junction. It is of considerable interest that in the same patient (D. H.) fourteen months after the onset of the disease, spinal anesthesia caused practically no change in limitation of passive motion. Correlated with this observation was the fact that hot foments had caused little improvement in the later stages in this patient. This suggests that changes in the muscle may be set up by persistent spasm, which eventually results in irreversible contracture.

These experiments indicate that the mechanism of muscle spasm in poliomyelitis is primarily neurogenic. Muscle spasm is apparently due to an increased discharge of motor nerve impulses from the spinal cord to the affected muscles. This is in keeping with the observation[3] that muscles in spasm in poliomyelitis exhibit increased electrical potentials. Elimination of this excessive discharge of motor impulses by spinal anesthesia or by block at the myoneural junction is effective in relaxing the spasm. While pain may be a factor of some importance in certain cases in increasing limitation of passive motion, it is not of primary significance in the etiology of spasm. It appears, rather, that the spasm produces the pain.

A neurogenic mechanism for muscle spasm is in accord with the accepted conception of poliomyelitis as a virus disease of the gray matter of the spinal cord. The virus is highly neurotropic and is selective in its attack on nerve cells of different types.[4] Furthermore, there is no inflammation or other pathologic change in muscle tissue in the acute stage of the disease, and virus is absent from the muscles.

It is unlikely that the associated meningitis can explain the persistent muscle spasm observed in poliomyelitis. The meningitis in this disease is mild, apparently lasts for only a short time, and virus is absent from the spinal fluid. Indeed, the suggestion has recently been made by Sabin[5] that the inflammatory cells in the spinal fluid in poliomyelitis may not represent a true meningitis but rather an overflow of cells from

the parenchymal inflammation of the spinal cord. Can the muscle spasm in poliomyelitis, which persists for months or years and which is more widespread than in severe meningitides, result from the brief mild meningeal irritation in this disease?

One is led to consider, therefore, that the muscle spasm as well as other signs and symptoms involving skeletal muscle in poliomyelitis may all be secondary to attack by the virus on neurons in the central nervous system.

A THEORY CONCERNING THE PATHOLOGIC BASIS OF MUSCLE SPASM

What is the pathologic lesion in the spinal cord which is responsible for the production of muscle spasm? A so-called "irritative lesion" of anterior horn cells would be difficult to reconcile with muscle spasm persisting for months after the acute infection. The persistence of the spasm suggests that the mechanism is more likely to be a "release phenomenon": a release from inhibition producing hyperirritability of the spinal mechanism for muscle tonus and proprioceptive reflexes.

Most pathologists emphasize injury and destruction of the large motor neurons in the anterior horn by the virus as the characteristic lesion in the spinal cord in poliomyelitis. There are a number of reasons for believing that involvement of anterior horn cells is not the pathologic basis of muscle spasm. In order to produce increased muscle contraction as in spasm, the anterior horn lesion would have to be "irritative," which is difficult to correlate with the persistence of spasm. Furthermore, destruction of anterior horn cells is invariably followed by denervation atrophy of muscle, while permanent atrophy does not occur in many muscles in spasm in poliomyelitis.

In order to determine the relationship of anterior horn cell pathology to muscle spasm, measurements were made of the chronaxie of muscles in spasm in fourteen of our poliomyelitis patients by Dr. J. Moldaver, of the Neurological Institute, New York. (By measuring the chronaxie of muscles in poliomyelitis, one may determine the degree of denervation of the muscle, and hence reconstruct the anterior horn cell pathology resulting from the virus infection.) It was found that many muscles in spasm in poliomyelitis have a normal chronaxie. Other muscles in spasm have a greatly increased chronaxie, suggesting marked anterior horn cell destruction. Still other muscles in spasm show partial neuromuscular degeneration which is apparently reversible. One may, therefore, conclude that there is no correlation between anterior horn cell destruction and muscle spasm in poliomyelitis. If we make the logical assumption of a unitary mechanism for muscle spasm in poliomyelitis, then an anterior horn cell lesion is ruled out by the fact that many muscles in severe spasm appear to have perfectly normal anterior horn cells.

Since an anterior horn cell lesion does not form a reasonable mechanism for the phenomenon of muscle spasm, one must cast about for another explanation. An enlightening suggestion has come from animal experimentation.

Muscle spasm similar in many respects to that observed in clinical poliomyelitis has been produced in dogs by a temporary arrest of the circulation to the spinal cord.[6] Following arrest of spinal cord circulation for forty-five minutes, the dog develops muscle spasm which persists unchanged for weeks. This muscle spasm is characterized by marked resistance to passive movement, pain on stretch of muscle, and pain on deep pressure, as well as loss or decrease of voluntary and reflex movement. Muscle spasm was observed in the posterior neck muscles, back, hamstrings, quadriceps, pectorals, latissimus dorsi, biceps,

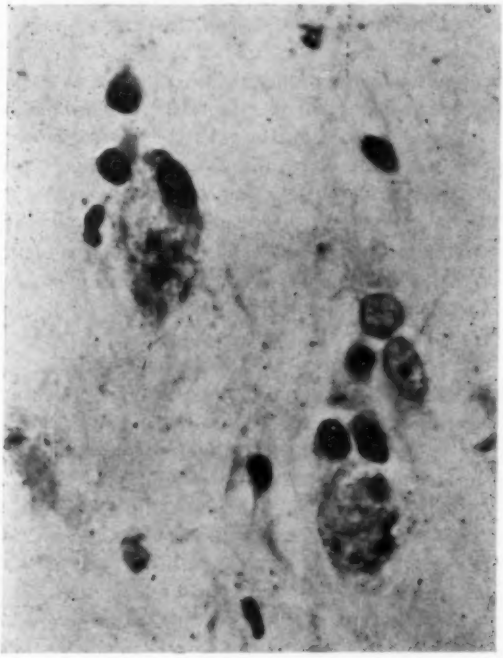

Fig. 1.—Dog subjected to arrest of spinal cord circulation for forty-five minutes three weeks previously. Intermediate zone of gray matter of spinal cord at sixth cervical segment. Marked injury and neuronophagia of internuncial neurons.

triceps, trapezius, and so forth, and was greater in the proximal than in the distal muscles. Both agonist and antagonist muscles were sometimes involved. In the forelimbs, reflex and voluntary movements were absent; in the hindlimbs, voluntary movement was absent but reflex movement was present. Sensation, autonomic functions, and respiration were normal. Examination of the spinal cord revealed a lesion localized to the region between the anterior horn and the posterior horn with marked injury and neuronophagia of the small internuncial neurons (Fig. 1). The large motor neurons in the anterior horn (Fig. 2), the preganglionic sympathetic neurons, and cells of nucleus dorsalis and of

the posterior horn were unaffected. The internuncial cell lesion was more severe in the brachial enlargement than in the lumbosacral enlargement of the spinal cord, correlating with the greater severity of muscle spasm in the forelimbs. Hypertonus has also been observed in cats as a result of a similar lesion.[7]

A lesion of internuncial neurons with some relatively normal anterior horn cells remaining would serve admirably as the pathologic basis of muscle spasm. Most of the synapses on the motor neurons of the anterior horn originate from the internuncial neurons.[8] Nerve impulses in the

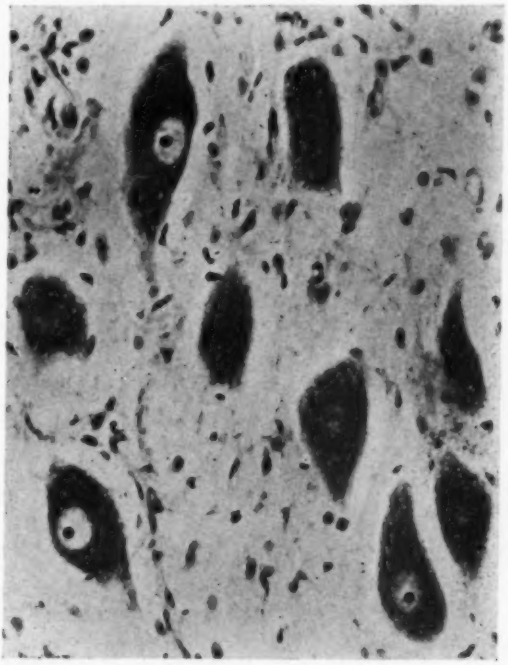

Fig. 2.—Same as Fig. 1. Anterior horn of spinal cord at sixth cervical segment. Note relatively normal anterior horn, large motor neurons.

pyramidal tract[9] and other tracts, as well as in many afferent nerve fibers, are relayed to the motor neurons of the anterior horn through the internuncial cells (Fig. 3). The internuncial neurons thus form the switchboard mechanism controlling the motor neurons. It is a reasonable hypothesis that a lesion of internuncial neurons may, therefore, produce a localized muscle spasm on the basis of release of anterior horn cells from inhibition. The characteristics of muscle spasm from an internuncial lesion would, however, differ from a typical upper motor neuron spasticity, because of the multiplicity of connections of the internuncial cells.

Thus far, it has been shown that muscle spasm may apparently be produced in animals by an internuncial cell lesion as a release phenomenon. One must still demonstrate that such a lesion occurs in human

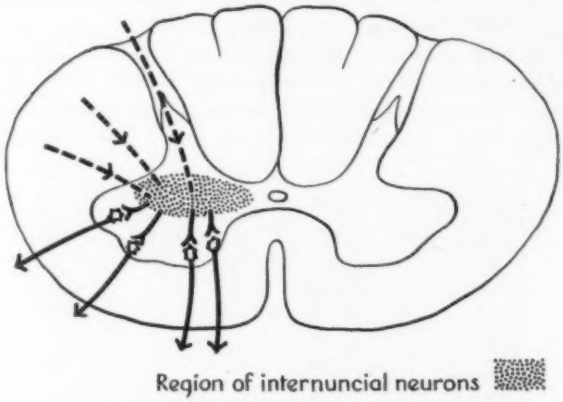

Fig. 3.—Diagrammatic drawing of a cross section of the cervical spinal cord showing the region of internuncial neurons with some of the afferent and efferent connections.

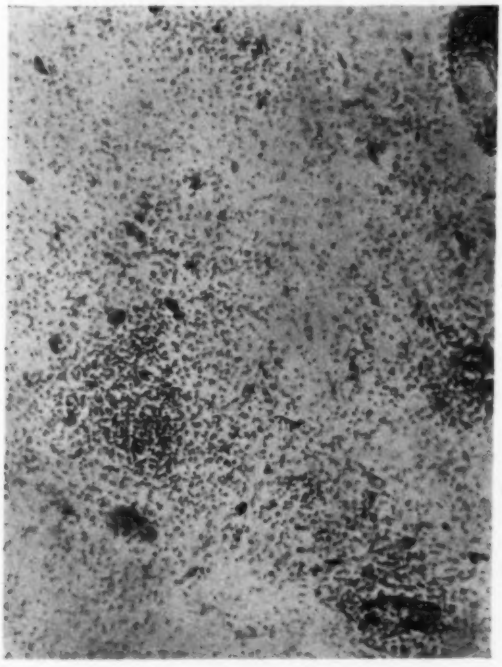

Fig. 4.—Human poliomyelitis. Intermediate zone of gray matter of spinal cord. Note inflammation in the region of internuncial neurons.

poliomyelitis and is correlated with muscle spasm. In analyzing the pathology of the spinal cord in poliomyelitis in man, one must keep in mind that only about from 5 to 10 per cent of the patients die in the acute stage, and it is this restricted group of the most severe cases which have received most attention from pathologists. Even in these very severe cases, however, it has been possible to find some patients who show a lesion of internuncial cells with relatively little damage to anterior horn cells.[10] In going over sections of the spinal cord from patients who died of poliomyelitis in the acute stage at Minneapolis

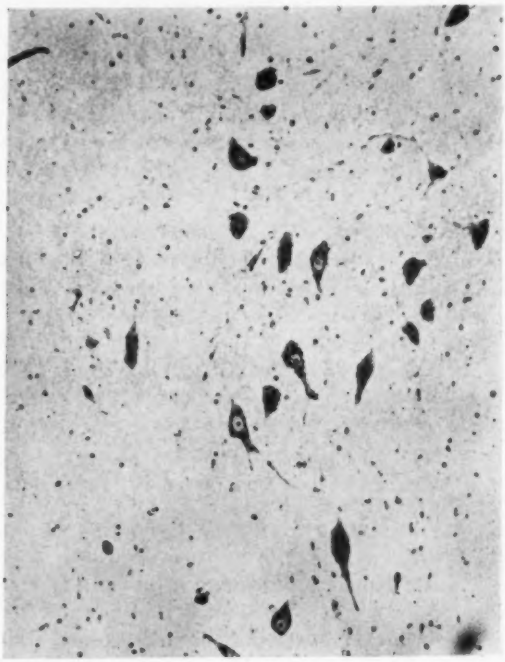

Fig. 5.—Anterior horn of spinal cord from human poliomyelitis. Note relatively normal anterior horn cells.

General Hospital, at the University Hospital, Aneker Hospital, and at the Mayo Clinic, twenty-six of sixty-eight patients showed predominantly inflammation and neuronophagia in internuncial neurons with relative sparing of anterior horn cells (Figs. 4 and 5). In the remainder of the sixty-eight patients examined, marked destruction of anterior horn cells as well as interununcial cells was observed. In one patient, who died in 1942, there was a record of severe muscle spasm correlated with a lesion of internuncial neurons and normal motor neurons in the anterior horn of the spinal cord.

Of considerable interest in this connection is the recent report of Minckler[8] on pathologic alterations in the synapses of the human spinal

cord in various neurologic diseases with the use of special staining methods. He studied eight patients with poliomyelitis and observed marked degeneration of the synaptic endings on the surface of the anterior horn cells (Fig. 6). He proved that injury to anterior horn cells themselves had no effect on synapses on their surfaces and concluded that the degeneration of synapses on the anterior horn cells was due to injury to the internuncial neurons. It is interesting to note that Minckler also reports two cases of tetanus in which the synaptic endings had practically disappeared from the anterior horn cells. Tetanus is, of course, characterized by severe "muscle spasm."

Fig. 6.—Pie diagrams showing proportion of degenerated synaptic endings in the spinal cord of normal individuals and of patients with poliomyelitis.

1. This schematic diagram of a hemisection of the gray matter of the thoracic cord shows the average percentages of granular forms (blackened sectors) of terminals ending in relationship to the cells of the principal nuclear groups in nonneuropathologic cases in patients under 30 years of age. The posterior sector in the gray matter represents the boutons around cells of the sensory and internuncial groups; the medial sector, of the nucleus dorsalis; the lateral intermediate sector, of the intermediolateral column; and the anterior sector, of the somatic efferent columns.

2. A diagram corresponding to *1*, but for nonneuropathologic cases in patients over 30 years of age.

3. The percentages of granular forms of terminals around cells of the principal nuclear columns in a thoracic field in a patient with poliomyelitis. (From Minckler, J.: Am. J. Path. 18: 1061, 1942.)

The observations of Minckler and our own studies on human pathology suggest that internuncial neurons appear to be frequently involved in poliomyelitis and that even in severe cases in which the patients die in the acute stage, the internuncial lesion may be more marked in some sections of the spinal cord than the anterior horn lesion. One may, therefore, assume that in the majority of patients who survive the acute infection, the internuncial lesion may actually predominate. In accordance with this view is the clinical observation that patients with mild poliomyelitis have muscle spasm but no paralysis, suggesting that internuncial neurons may perhaps be more sensitive to the virus of poliomyelitis than anterior horn cells in the spinal cord.

One question that remains is why the internuncial lesion should eliminate inhibitory mechanisms without blocking impulses for excitation of muscle tonus and stretch reflexes. A recent observation of Lloyd[11] helps to explain this phenomenon. He has demonstrated that the proprioceptive reflex arc in the cat is a two-neuron arc, with no interposed internuncial neuron. Therefore, the nerve impulses for excitation of tonus and stretch reflexes would be conducted through the internuncial region only by nerve fibers. Since nerve cell bodies are

susceptible to the virus of poliomyelitis but nerve fibers do not appear to be attacked directly by the virus, excitation of the proprioceptive reflexes would not be blocked by virus involvement of the internuncial region. On the other hand, since impulses for inhibition of tonus and stretch reflexes are conducted through the internuncial neurons, the attack by the virus on these neurons would lead to an exaggeration of proprioceptive reflexes, as a result of release from inhibition.

From these observations, a conception of spinal cord pathology emerges which is characterized by two types of lesions: (1) an anterior horn cell lesion resulting in motor denervation with muscle atrophy and (2) an internuncial lesion resulting in muscle spasm. The two lesions show great variability in their distribution, so that one may see, in different muscles, muscle spasm with or without denervation atrophy and motor denervation with no muscle spasm. It appears probable that some functional anterior horn cells must remain to produce clinical muscle spasm.

Another possible mechanism for muscle spasm that suggests itself would be based on acetylcholine contracture. It is well known that denervated muscle is hypersensitive to acetylcholine.[12] Acetylcholine readily produces contracture in denervated skeletal muscle.[13] The possibility that acetylcholine contracture might play a role in muscle spasm in poliomyelitis has been investigated by the study of the effects of prostigmine on muscle spasm. This drug exaggerates the action of acetylcholine by inhibiting cholinesterase at the myoneural junction. If prostigmine resulted in an increase in hypertonus, one would have to consider acetylcholine contracture as a possible factor in the mechanism of muscle spasm. However, prostigmine produced relaxation of muscles in spasm in patients with poliomyelitis.[14] This observation suggests that acetylcholine contracture is not the basis for muscle spasm in this disease.

The relaxation of muscle spasm in poliomyelitis by prostigmine is apparently based upon the action of the drug on the spinal cord, inhibiting the centers for proprioceptive reflexes.[14, 15] There is evidence that the locus of the spinal action of these drugs is proximal to the anterior horn cells, presumably on the internuncial neurons.[16] The relaxing action of prostigmine on muscle spasm provides additional support to the theory that an internuncial lesion, by interfering with inhibition at synapses on the anterior horn cells, is responsible for muscle spasm in poliomyelitis.

Interference with the conduction of impulses through the internuncial switchboard to the motor neurons in the anterior horn may also help to explain the phenomenon of "incoordination" in poliomyelitis. This appears to be essentially a disorganization in the flow of impulses to anterior horn cells, resulting in involuntary contraction of antagonistic and synergistic muscles. There is also disorganization in discharge of motor impulses to muscle fibers within a single muscle, resulting in

fascicular twitchings in voluntary and reflex contraction of the muscle. Incoordination is decreased by prostigmine[14] and by muscle re-education.

SUMMARY

1. Muscle spasm in poliomyelitis is of two types:

A. Hypertonus

B. Hyperirritable stretch reflex

2. The clinical characteristics of muscle spasm are described.

3. Muscle spasm is relaxed temporarily by spinal anesthesia or block of the myoneural junction in acute and subacute poliomyelitis. Intravenous pentothal decreases muscle spasm moderately in some patients and is ineffective in other patients.

Muscle spasm in poliomyelitis has a neurogenic mechanism and is apparently the result of an increased discharge of nerve impulses through the motor neurons.

4. Evidence is presented to support the theory that the pathologic basis of muscle spasm in poliomyelitis is a lesion of internuncial neurons in the gray matter of the spinal cord. The muscle spasm is produced as a result of release of proprioceptive reflexes from inhibition.

A. Muscle spasm has been produced in the experimental animal by temporary arrest of circulation in the spinal cord. Correlated with this muscle spasm, the spinal cord showed a lesion localized to the internuncial neurons, while the anterior horn cells appeared normal.

B. In sixty-eight cases of poliomyelitis, review of the spinal cord pathology revealed an internuncial lesion in almost every patient. Twenty-six patients showed an internuncial lesion with relatively normal anterior horn cells.

C. Measurements of chronaxie of muscles in fourteen patients with poliomyelitis who exhibited marked muscle spasm demonstrated that there is no correlation of muscle spasm with anterior horn cell damage. Many muscles in spasm showed a normal chronaxie while other muscles in spasm showed more or less marked increases in chronaxie. These results suggest that anterior horn cell destruction is not the basis of muscle spasm in poliomyelitis.

D. Prostigmine, acting on the spinal cord to inhibit proprioceptive reflexes, relaxes muscle spasm and may be of therapeutic value in poliomyelitis.

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TRAUMATIC CARDIAC INJURY IN A CHILD WITH PROBABLE RUPTURE OF INTERVENTRICULAR SEPTUM

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THE case here presented is one of cardiac trauma in a child, due to a nonpenetrating injury of the chest, associated with the sudden onset of a loud, rather striking murmur and thrill.

Two recent, fairly extensive and thorough reviews of nonpenetrating wounds of the heart and pericardium have been written by Bright and Beck[1] in 1935 and Warburg[2] in 1938. Kahn and Kahn[3] wrote an earlier review of the problem in 1929 and set forth criteria for evaluating the disability involved.

Bright and Beck's review of the available literature in 1935 disclosed 168 cases, of which 12 patients survived, 152 died of rupture of the heart, and 11 died of congestive failure. Of those who died of rupture, the right auricle was involved thirty-six times; the left auricle, thirty times; the right ventricle, thirty-one times; and the left ventricle, thirty-seven times. The interventricular septum was ruptured eleven times and the auricular septum once.

Warburg collected cases of 197 patients with post-mortem material available on fifty-one. Of these, the auricles were involved seven times, and the ventricles, twenty times; the interventricular septum was injured in four instances, ruptured in one. "Affections of the pericardium were frequent."

CASE REPORT

R. V., a Negro boy, 11 years old, was admitted to St. Luke's Hospital on Jan. 5, 1943.

While out sledding, the patient was hit by an automobile and lost consciousness for a short period of time. On admission to the hospital he complained only of a headache and severe pain in the left upper quadrant of his chest.

Examination revealed a frightened and hurt child, lying on his right side with his knees drawn up. There were no neurologic findings. His abdomen was tense. Tenderness in the epigastrium was marked, but the findings were not held to be pathognomonic of a ruptured viscus. There was a small scratch on his chin, but otherwise there were no contusions or lacerations.

His heart on admission, one and one-half hours after the accident, exhibited a marked systolic thrill which could actually be seen to produce vibration of the chest wall, and a harsh murmur, limited to systole, which was heard over the whole precordium. Heart size was normal to percussion. His blood pressure was 110/80 and his pulse, 100. Pressure on the thoracic cage did not reveal any tenderness.

From the Children's Cardiac Service of St. Luke's Hospital.

His past history was negative for rheumatic fever. He was born in St. Luke's Hospital and had been repeatedly observed in the clinic (forty-two times) from birth to 7 years of age and his heart was consistently noted to be normal.

He slept that night and henceforth was symptom-free, all abdominal pain having subsided. He appeared to be entirely recovered.

Cardiac consultation was requested and our findings were as follows: The patient had a systolic thrill and a systolic murmur, harsh and maximal just to the left of the sternum, in the fourth interspace. No presystolic or diastolic murmurs. Third heart sound at apex. Possible slight enlargement. It was suggested that an electrocardiogram and two meter chest films be made. Impression: Congenital interventricular septal defect or ruptured septal defect due to trauma.

The laboratory findings revealed an erythrocyte count of 4,800,000; a leucocyte count of 11,700, and a sedimentation rate of 2.5 mm. by a modified Westergren method (normal 0 to 5 mm.). Urinalyses were negative for blood, showed a small amount of albumin, and, on one occasion, granular casts were reported.

The chest x-ray picture showed fullness in the region of the pulmonary conus with some increase in the root shadows on both sides, felt to be due to passive congestion. The heart did not appear to have a mitral lesion, but was more probably congenital. It occupied 45.5 per cent of the transverse diameter of the thoracic cavity.

The electrocardiogram showed a rate of 110 with a normal sinus mechanism, a P-R interval of 0.16; Q-S interval of .06, and a QRS-T interval of .28. QRS groups in the classic leads were low; II and III showed large Q waves. This was felt to be compatible with a congenital defect.

The boy's temperature reached 101° F. on the third hospital day and on the seventh day was normal. He was then discharged to be seen in the cardiac clinic.

When seen in the clinic on January 22, seventeen days after his accident, the murmur was noted to be shriller and more musical in quality, like a crow call. Another sedimentation rate was normal, but an electrocardiogram showed a remarkable change, primarily in the T waves, indicating diffuse myocardial damage, mainly in the posterior wall. There was, in addition to a Q in Leads II and III, an elevated S-T in IV, and deeply inverted T waves in II, III, and IV.

Admission to the hospital was advised with a provisional diagnosis of contusion to the myocardium and rupture of the interventricular septum.

The second hospital admission was Jan. 22, 1943. An interval note revealed that he had wrestled with his brothers and thrown snowballs at home, although he had been kept out of school. He had been only very slightly short of breath, had never noted any substernal distress of any sort, and complained only of a little "sticky pain" over his apex. This pain was not related to exercise nor relieved by rest, except that it was said to be most marked when he was tired. It was transient and short-lived.

The physical examination was negative, except for the findings in the heart. The lungs were, and remained, quite clear; râles were never heard.

The following description was made of the cardiac findings:

A diffuse apical impulse was seen in the fourth and fifth interspaces, about 6 cm. from the midsternal line. A thrill, limited to systole, was palpable over the entire precordium and to the right parasternal line and was maximal in intensity just to the left of the ensiform process in the fifth interspace. The left border of dullness was approximately 7.5 cm. from the midsternal line, about 1.25 cm. to the left of the midclavicular line. A musical, very loud, systolic murmur (like a rain crow) was heard over the entire chest, anteriorly and posteriorly, louder over the precordium, and loudest to the left of the sternum in the fifth interspace. It was not transmitted up into the neck but was heard well in both axillae. At the

base, over the pulmonic area, the murmur was obliterated by a harsh, rumbling, rolling, systolic murmur. No diastolic murmurs were anywhere present. M_1 was replaced by the murmur, and M_2 was faint. P_2 was very loud and snapping, could be felt with the finger tips, and was very much greater than A_2. The first sounds at the base were replaced by the murmur. Blood pressure, 95/68; pulse, 100.

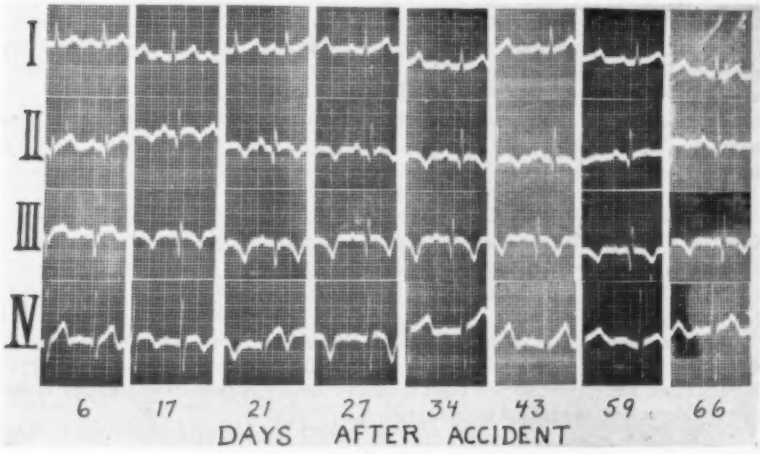

Fig. 1.—First eight electrocardiograms.

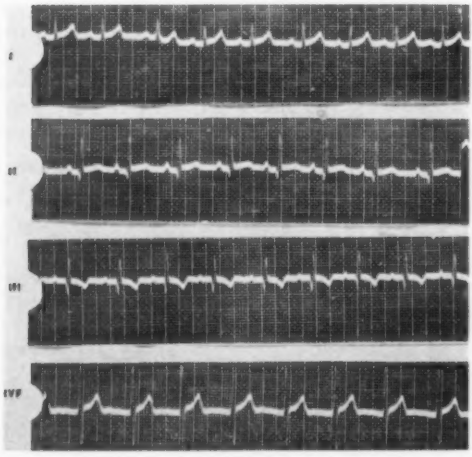

Fig. 2.—Electrocardiogram taken 129 days following accident.

Laboratory examination showed a normal erythrocyte count, slightly elevated leucocyte count, and normal differential. The urinalysis was normal.

The patient remained in the hospital twenty-nine days and was afebrile throughout, except on his sixth, seventh, and eighth hospital days when he had some transitory abdominal pain and an elevation of the white blood count to 20,100. At that time his sedimentation rate was normal.

Two more chest films were made, and one stethographic and five electrocardiographic tracings were taken during this admission.

In the first x-ray picture of the chest, taken three weeks after the patient's accident, his heart occupied 44 per cent of the transverse diameter of the chest and had the same general configuration as the film taken on the first admission. The left side of the heart measured 7.7 cm. The second chest plate was taken six weeks after the accident and showed the heart and vascular markings to be essentially unchanged and the heart to occupy 46.3 per cent of the thorax. The left side of the heart measured 7.2 cm.

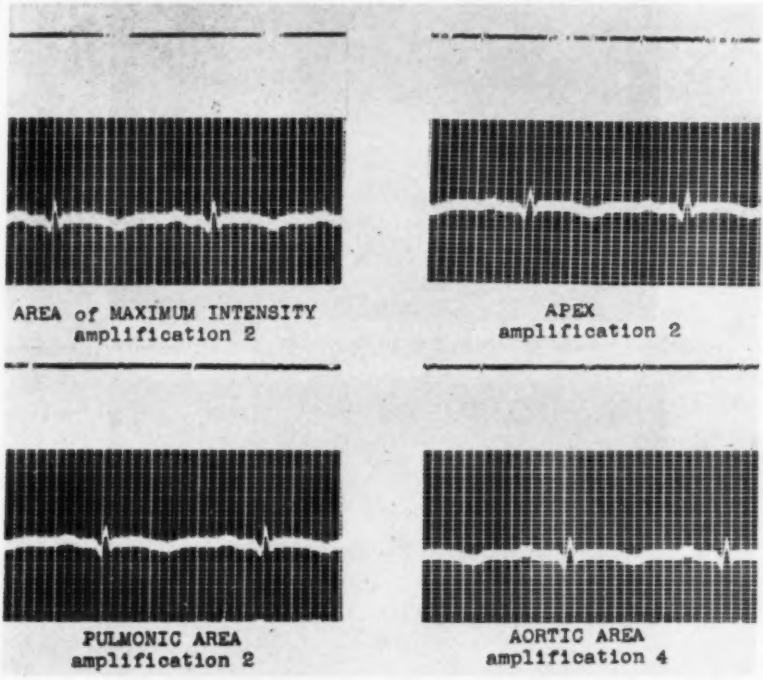

Fig. 3.—Stethographic tracing taken Jan. 27, 1943, twenty-two days after accident.

Electrocardiograms were taken on the seventeenth, twenty-first, twenty-sixth, thirty-third, and forty-fourth days following the accident.

These all showed progressive changes back toward a normal configuration; abrupt in the fourth lead, gradual in the second, and only slight in the third, with a marked Q wave and an inverted T wave continuing to mark the site of maximal injury.

The T wave in the fourth lead reverted to the upright position in the tracing taken on the thirty-third day.

The stethographic tracing, taken on January 27, twenty-two days after the accident, demonstrated a long murmur, filling systole, with no diastolic murmur, but a third heart sound present in the apical lead.

The patient was discharged from the hospital, to be followed in the cardiac clinic, on Feb. 20, 1943, twenty-nine days after his second admission and forty-seven

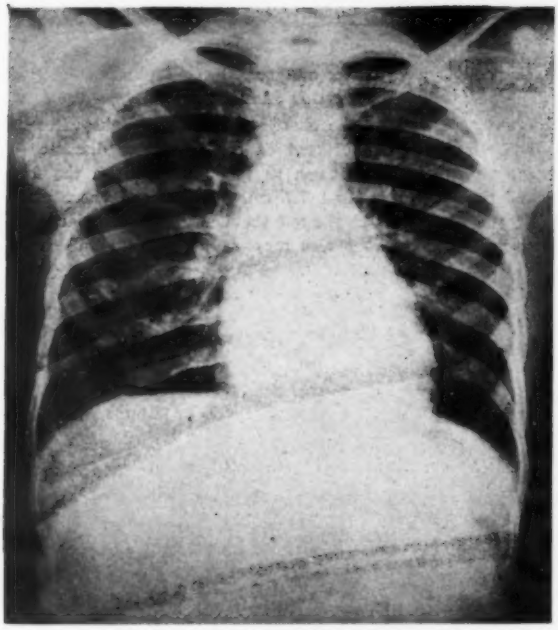

Fig. 4.—X-ray picture on first admission, six days after accident.

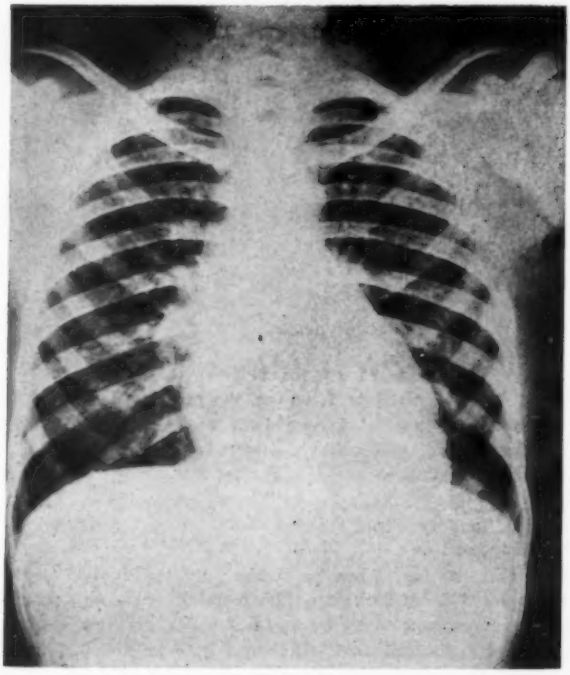

Fig. 5.—X-ray picture taken on April 8, 1943, ninety-three days after accident.

days after the accident. He felt well and had suffered no pain of any description in the chest during the last three weeks of his hospitalization.

He has since been seen four times in the clinic, where his sedimentation rate and leucocyte count continued to be normal, and has had three electrocardiograms taken, the last, 129 days following the accident. These showed a continuation of the healing process with a complete return to normal of the second lead and a less pronounced Q_3, T_3.

The patient has returned to regular school, and although his attendance can only be called irregular at best and although he tires easily, he does seem to be about as strong and well as he ever was, having always been a "weak" child. At no time has he complained of dyspnea.

DISCUSSION

In the present case the diagnosis of recent trauma to the heart due to a nonpenetrating wound to the chest is firmly established on the basis of the patient's age, history of injury, lack of previous cardiac history, the appearance of a significant murmur and thrill not found to be present on earlier examinations, and progressive changes in serial electrocardiograms. The electrocardiograms indicate actual contusion of the muscle wall itself.

However, that the damage was not limited to the myocardium is established by the sudden appearance of a marked systolic murmur and thrill. Several possible causes of this murmur were considered: (1) rupture of the interauricular septum; (2) rupture of the right anterior sinus of Valsalva into the right ventricle; (3) rupture of the aortic valve; (4) traumatic pericarditis; (5) rupture of the mitral value; (6) rupture of chordae tendinae; (7) rupture of papillary muscles; and (8) rupture of the interventricular septum.

Taking these in order, it is immediately apparent that the timing, character, and location of a murmur due to a ruptured auricular septum, sinus of Valsalva, or aortic valve excludes them from further consideration inasmuch as such lesions would produce basal diastolic murmurs.

The remaining possibilities, however, must be more carefully considered.

The very early, abrupt onset of the murmur (known to be present one and one-half hours after the accident), its character, and persistence speak most strongly against its being due to a pericardial friction rub. The latter usually appears days to weeks later and subsequently disappears, although one report[4] states that it may be noted as early as from six to twelve hours after the injury.

The customary electrocardiographic picture of an acute pericarditis is inversion of the T waves in the classical leads and upright in lead IV. The S-T segments have a low take-off, and the Q waves in I and III are not exaggerated.

The patient presented an upright T wave in I and sharp inversion in Leads II, III, and IV, high S-T in Leads II and IV, and markedly exaggerated Q waves in II and III.

The shape of the heart and its constancy as shown by x-ray films do not support a pericardial effusion which usually follows.

And finally there was no precordial pain of consequence at any time.

Mitral value rupture is usually secondary to pre-existing valvular disease,[5-8] and when it does occur, respiratory distress is almost immediate[9] and much more prominent than the cardiac findings. In fact the patient may die of pulmonary edema without ever having developed any murmurs.[8]

When a murmur is heard, it is usually in the mitral area, systolic in time, low toned, musical, sonorous,[5] and unaccompanied by a thrill.

The prognosis is extremely poor and most patients succumb within a few hours to days.

Rupture of chordae tendinae is recorded occasionally.[10-17] In two instances it was held to be due to trauma. One dying and coming to autopsy[13] had a harsh systolic murmur, but no thrill. Necropsy disclosed that four chordae were ruptured from the middle two-thirds of the posterior mitral leaflet. In the other case[14] a "low pitched, vibrating murmur at the apex and to the left of the sternum was heard which sounded like a jew's-harp." It was systolic in time; there was no thrill. Two years later a soft, transitory thrill appeared for a few days.

Vasquez[5] describes the murmur due to rupture of chordae tendinae thusly: "A systolic murmur, very low in pitch and like a jew's-harp in character, heard over the middle of the heart."

In 1935, Stevenson and Turner[18] reviewed the literature on spontaneous rupture of papillary muscles, collected nineteen cases, and added one of their own. Since then there have been at least three[19-21] more cases added. An analysis of the murmurs found in this group of twenty-three patients is made in Table I.

TABLE I

	NUMBER OF CASES
No murmur	3
No murmur noted	9
Systolic and diastolic	3
Systolic at apex	2
Systolic at base	2
Systolic "in axilla"	1
Murmurs	1
"Loud noises over precordium"	1
Whistling diastolic at apex	1

No thrills were noted in any of the patients in these cases.
Thirteen very shortly developed respiratory distress.
Almost all died within a matter of hours after the actual rupture occurred, but one patient lived twenty months in congestive failure.

In 1937, Payne and Hardy[22] recorded what they believed to be the first case of traumatic rupture of a papillary muscle. However, Glendy and White[23] had reported a case in a 24-year-old youth who died of a ruptured spleen. In neither instance was a murmur heard, and both were confirmed at autopsy.

Sager,[24] in 1934, reviewed the existing literature on acquired defects of the interventricular septum due to coronary disease, found seventeen cases, and added one of his own. Since then cases have been reported by many others.[25-31]

An analysis of the condition of this group of twenty-five patients is made in Table II.

TABLE II

	NUMBER OF CASES
No murmur noted (5 were reported between the years 1845 and 1906)	6
Loud, rough, shrill or harsh systolic murmur	19
Systolic thrill	15
Soft diastolic	2

In the nineteen patients in whom murmurs were noted, there were ten in whom no point of maximum intensity was located; the murmurs were stated merely to be heard over the whole precordium. In seven patients the point of maximum intensity was in the fourth and fifth interspaces just to the left of the sternum. In two it was noted to be maximal at the apex.

In one patient[26] "the thrill was very accessible and the murmur intense." In another[25] a thrill was felt to the left of the sternum and there was heard "a marked systolic murmur of musical quality over the entire precordium." Bayley and Fader[29] describe a loud, rough murmur, medium in pitch, lasting throughout systole, and heard best in the fourth and fifth interspaces 3 cm. to the left of the sternum and transmitted over the entire precordium. "A pronounced thrill" was felt over the lower precordium and to the left of the sternum. Stanley[30] noted a loud, harsh, systolic murmur with a thrill located in the fourth interspace just to the left of the sternum.

Sager[24] typifies the auscultatory findings as "a harsh systolic murmur and a rough systolic thrill over the precordium with their maximum intensity to the left of the sternum in the fourth and fifth interspaces. It is usually transmitted to the left axilla and subscapular region, but not to the great vessels."

Cases of acquired interventricular septal defect due to trauma with clinical notes were hard to find, since most of the patients died almost instantly.[32-35] But one that lived long enough to be described[36] was noted to have a systolic thrill and a very loud systolic murmur masking all heart sounds, maximal at the apex.

Anderson[4] reported a case of a 30-year-old white man who was stepped on by a horse and was found to have a loud systolic murmur heard over the whole precordium, loudest in the fourth interspace to the left of the sternum, associated with a faint systolic thrill. No second sound was audible except P_2. He went into mild failure and developed a friction rub which later disappeared. His heart was enlarged by x-ray and his electrocardiogram showed elevation of the S-T segments and inversion of T_2. Rupture of the interventricular septum was held to be the lesion accountable and one year later he was taking all sorts of exercise without any shortness of breath.

From our own experience and from published reports, we feel confident that this patient's murmur was due to a rupture of the interventricular septum. Whether the change in pitch of the murmur between the first and second hospital admissions was due to a narrowing or an enlarging of the opening or a diversion of the stream consequent upon a gradual yielding of contused tissues or to some other cause cannot be determined, but it in no way mitigates against the diagnosis of rupture of the interventricular septum.

It is of some interest to note also that when Bright and Beck[1] injected blood into the interventricular septa of dogs they got deep Q waves in Leads II and III, inverted T in I, II, and III, and a high take-off of S-T in II and III.

SUMMARY

A case of contusion to the heart due to a nonpenetrating injury in an 11-year-old boy is presented and the additional diagnosis of rupture of the interventricular septum is made from an analysis of the history and physical findings and review of the literature.

Such occurrences are rare, survival unique.

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LATE EFFECTS OF SEVERE ASPHYXIA NEONATORUM

A Preliminary Report

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THIS study attempts to determine whether an objective statistically significant difference in mental status exists between children severely asphyxiated and apneic at birth and their siblings or parents.

Asphyxia neonatorum as a specific disease entity is nonexistent. It is a clinical term commonly used to designate the manifestations of anoxia which result from obstruction to placental or fetal circulation, obstruction to fetal respiratory passages, narcosis, prematurity, abnormal delivery trauma, maternal anemia, maternal fever, rapid labor, instrumental delivery, long second-stage labor, or premature rupture of membranes.[2, 20, 23, 24, 26]

Asphyxia may be classified as peripheral or central, depending upon whether the anoxia is a resultant of factors operating peripherally or directly upon the respiratory center. Anoxia may be subdivided into anoxic anoxia, resulting from a lack of oxygen; anemic anoxia, resulting from a reduced oxygen-carrying capacity in the blood (diminution of hemoglobin, carbon monoxide poisoning, methemoglobinemia); stagnant anoxia, resulting from slowing of the circulation or diminution in effective circulating blood volume; and histiotoxic anoxia, resulting from inability of the cells to utilize oxygen.

PHYSIOLOGY

The respiratory quotient of nervous tissue is higher than that of any other body tissue. A gradient in respiratory quotients is found in nervous tissue as follows: cortex, .99; brain stem, .93; cerebellum, .89; medulla, .89.[21, p. 330] "Cerebral tissue utilizes 9.5 to 10 c.c. of oxygen per 100 Gm. per minute . . . far above other organs . . . twenty times that of resting muscle."[21, p. 326] Gomez and Pike[31, p. 982] found that the cells of the cerebrum suffered permanent damage after eight minutes of anoxia; the Purkinje cells of the cerebellum showed diffuse chromatolysis after thirteen minutes, and cells of the vital medullary centers, after from twenty to thirty minutes. More recently in an excellent study it has been shown[31] that by clamping the pulmonary artery in cats permanent alterations in behavior and psychic function occurred in animals subjected to three minutes and twenty-five seconds or more of circulatory arrest. Permanent pathologic lesions were seen to occur in animals subjected to three minutes and ten seconds of complete arrest of the circulation. Many observers[3, 4, 8, 17, 31, 32] have shown that anoxia may

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produce definite pathologic cerebral lesions. Exposure to a mixture of from 5.5 to 6 per cent oxygen and nitrogen did not produce sufficient anoxemia to result in brain lesions in kittens.[15]

When the mean oxygen unsaturation of capillary blood, which normally ranges between 3 and 4 volumes per cent, reaches 6.5 volumes per cent, cyanosis results.[9] "The low oxygen content of the fetal blood and its high oxygen unsaturation will be still further accentuated if we consider the various anatomical 'shunts' of the fetal circulation. The blood supplying the (fetal) brain will contain less oxygen than the umbilical vein blood due to its admixture with blood returning from the lower extremities. The very high unsaturation of fetal blood in respect to oxygen indicates that the full-term fetus in utero exists normally in a state of cyanosis.[9]

The fetus in utero does not normally experience oxygen want despite the cyanosis, as shown by studies of the lactic acid content of fetal blood.[10] Hence there may or may not be a relationship between anoxia and cyanosis.

In asphyxiated infants an oxygen content of umbilical vein blood of 1.3 volumes per cent is found, and irreversible changes are found with 1 volume per cent oxygen and a blood lactic acid over 60 mg. per cent.[9, 10, 12]

The increased hydrogen-ion concentration indicated by the change in pH[10] acts upon the cerebral vessels and results in a further lessening of oxygen supply by "congestion of cerebral vessels, cerebral edema, and increased cerebrospinal fluid pressure. This occurs even in cases of mild carbon monoxide asphyxia and is very severe in prolonged fatal cases."[8]

One of the most interesting and pertinent recent findings related to the problem of fetal anoxia is the finding of Snyder and Rosenfeld,[28, 29] that the movements of respiration occur rhythmically during the latter one-third of intrauterine life and that once these movements are established they are continuous unless some strong influence is exerted upon the fetus. If the infant does not take its first extrauterine breath within a few seconds after delivery, it has been profoundly affected and the respiratory rhythm has been upset.

The physiology of nervous tissue indicated in preceding paragraphs shows that anoxia should detrimentally affect the cortical cells of the cerebrum without having as detrimental an effect upon the vital centers. The present study was made in an effort to answer the question, Does the destruction of cortical cells with no replacement result in retardation of mental development without any other evidence of neurologic sequelae?

RELATED STUDIES

Schreiber[25] noted that 70 per cent of a large group of children having brain defects were found to have been asphyxiated at birth.

Brander[1] finds a relationship between twin births, first born, forcep deliveries, and mental deficiency.

Hess[18] and co-workers in an excellent study found that premature birth, unassociated with evidence of intracranial injury, does not affect mental development. This finding, coupled with the high incidence of cyanosis in premature infants, serves to re-emphasize the fact that cyanosis may not be indicative of anoxia.[2, 9, 10, 20]

Dayton,[7] in an analysis of abnormal labor as an etiologic factor in mental deficiency, studied reports of 20,473 cases. He found some relationship between abnormal labor and individuals in the dull normal group (I.Q., 90 plus). No association was found between abnormal labor and the groups with I.Q.'s of from 0 to 29 and from 80 to 89. The data for this study[7] was secured by means of verbal report five to sixteen years after the birth of the children.

McPhail and Hall[19] conclude that "apnea may be present at birth without severe anoxia and its resultant cerebral damage, providing oxygen is administered during the apneic period." With the preceding statement there can be no disagreement. It is obvious that for cerebral injury to occur, the apnea and resultant anoxia must be of a certain length of time and of a degree sufficient for permanent cell damage to take place. The mental retardation which obtains in asphyxiated infants is directly dependent upon the degree of cerebral oxygen impoverishment.* Previous studies of this problem have been made on infants less severely anoxic than those used in this study. The criteria for "severe apnea" as given by one investigation[19] is (1) "both breathing and crying are delayed for more than one minute" or (2) "all babies developing cyanosis in the first few days of life are considered to be severely apneic." The cases[19] of "severe apnea" are drawn from a total of 1,097 cases. Two hundred and seventy patients were able to be followed, of whom eleven (4.1 per cent) were considered to be severely apneic by the criteria as given. Cyanosis is caused by an increased amount of reduced hemoglobin in the capillaries of the skin and mucous membranes and develops clinically when a sufficient amount of oxygen unsaturation develops in the blood (6.5 volumes per cent). The occurence of cyanosis may bear no relationship to severe anoxia.[2, 10, 20] Case 3 in the present study is an excellent case for illustrating this point.

MATERIAL FOR PRESENT STUDY

The cases used in the present study were drawn from a total number of 25,261 deliveries (New York Hospital, 13,740; University of Pennsylvania Hospital, 11,521).

By searching the hospital records of the University of Pennsylvania Hospital† twenty-six cases of the most severely asphyxiated new-

*See page 157.

†Courtesy of Dr. Joseph Stokes, Professor of Pediatrics, University of Pennsylvania, School of Medicine.

born infants who survived birth and hospital period following were secured. In most cases of comparable severity, judging from the hospital records, the infants did not survive. The severity of the degree of asphyxia may be judged by referring to Table I. Twenty-three similar cases were secured from the hospital records of New York Hospital* from the years 1932 to 1939. Because of the time interval necessary to elapse before reliable mental measurements could be made of these children, many could not be located at the time of the follow-up study. A resultant fourteen cases from the University of Pennsylvania Hospital and five cases from New York Hospital constitute the cases concerned in this study. The ages of the asphyxiated children at the time of the follow-up examination varies from 2 years, 5 months, to 11 years, 8 months. A parent or sibling of each asphyxiated child was examined to form the control group.

The criteria for the selection of cases follow:

1. No positive neurologic findings were present at the time of birth, during the neonatal period, or at the time of the follow-up examination.

2. Only children who were severely asphyxiated were selected for follow-up examination. An effort was made to obtain cases of children who had had asphyxia pallida or who were definitely stated to have been apneic for a period of three minutes or longer. These infants must have survived and met criterion 1.

3. In an effort to obtain cases in which damage in the infant, if present, might more likely have been attributed to anoxia, those selected were cases in which the attending physicians during the birth and the neonatal period of the infant did not diagnose or suspect intracranial hemorrhage.

All cases meet the first criterion.

The first ten cases (Group A) exactly met the second criterion as to degree of asphyxia. The next four cases (Group B) met the degree criterion by inference from the birth histories (Table I). The last five cases (Group C) included those children with severe asphyxia which did not progress to asphyxia pallida and in whom no objective statement as to the period of apnea was given. Table II is a chart showing the relationship between the intelligence quotients of the asphyxiated children and their controls in these three groupings. The mean I.Q. of the children in Group A was 87 (mean control, 99.3). The mean I.Q. of the children in Group B was 77 (mean control, 99.7). The mean I.Q. of the children in Group C ("severely asphyxiated" children with no duration of apnea given) was 98.4 (mean control, 103.4).

The difficult problem of excluding cases of intracranial hemorrhage (criterion 3) remains, and how successfully it was met is not known. Craig,[6] in a study of 126 cases of intracranial hemmorrhage, which terminated fatally, found 48 cases in children in whom intracranial hem-

*Courtesy Dr. S. Z. Levine, Professor of Pediatrics, Cornell University Medical College, and Dr. G. W. Wheeler, Superintendent of the New York Hospital.

TABLE I

CASE	ASPHYXIA		HOW REVIVED	INCIDENTAL TO DELIVERY	I.Q. OF ASPHYXIATED INFANT	I.Q. OF CONTROL (SIBLING OR PARENT)
	DEGREE	DURATION				
1	Severe (asphyxia pallida); apnea relaxation of mouth and extremities; reflexes absent; glottis closed; heart rate, 40; considerable meconium in hypopharynx	Twenty minutes	Flagg apparatus used to remove mucus; after prolonged artificial respiration, the child took several breaths spontaneously	Anterior parietal; membranes ruptured at 4:35 P.M. and shortly thereafter fetal heart became faint and irregular (rate, 68); birth 6:15 P.M.; cord pulsation absent at birth	48	95
2	Marked (asphyxia pallida)	Baby cried within two minutes after delivery and then ceased breathing and progressed to asphyxia pallida; heart rate, approximately 40	Coramine, 1 c.c.; CO_2-O_2	Normal L.O.A.; premature; cord about neck	52	70
3	Mild cyanosis	Child made no respiratory efforts for fully eight minutes after delivery	Milking of trachea; aspiration; Drinker respirator; lobeline	Normal; progressive slowing of fetal heart rate during four hours prior to birth; cord normal	76	101
4	Marked	Approximately five minutes	Placed in Drinker respirator without success; Foregger intratracheal administration of CO_2-O_2	Persistent R.O.P.; mid-Simpson's forceps rotations; cord normal	118	132
5	Asphyxia pallida	Ten minutes	CO_2-O_2 and Drinker respirator	Persistent R.O.P.; outlet forceps and rotation of head on perineum; cord normal	98	104

6	Marked	"Did not breathe for five minutes. Foul odor"	Aspiration; CO_2-O_2; artificial respiration	Normal L.O.A.; premature; rupture of membranes (54 hours); cord about neck with prolapsed right arm tangled in cord and resting in nuchal position	77	78
7	Moderate, somewhat pallid and with little muscle tone	No statement	CO_2-O_2; lobeline; maternal blood intramuscularly	R.O.P.; obstructed at outlet for seven hours; cord normal	112	102
8	Third degree	"Not breathing and did not respond to usual method of resuscitation. With exception of an inspiratory gasp (not more than once every two or three minutes) the baby still refused to breathe. 25 minutes later the gasps were a little more often"	Aspiration of considerable mucus; intratracheal intubation CO_2-O_2; alpha lobeline, maternal blood intramuscularly	Persistent R.O.P.; forceps rotation; Scanzoni; cord normal	104	110
9	Marked	Artificial respiration for four minutes before baby cried		Normal; cord once around neck	93	107
10	Severe, irregular respirations; no reflexes obtainable except Chvostek	No statement	Aspiration of considerable mucus; cried after aspirated; poor respiratory excursions	Placenta previa; version and breech extraction; Piper forceps; fetal heart not heard before delivery	92	94
11	Baby had continuous convulsions at 16 hr. of age, lasting for four hours (becoming black at times)	No statement	Aspiration of mucus	Mother had rheumatic mitral stenosis and decompensated during delivery	113	126

TABLE I—CONT'D

CASE	ASPHYXIA		HOW REVIVED	INCIDENTAL TO DELIVERY	I.Q. OF ASPHYXIATED INFANT	I.Q. OF CONTROL (SIBLING OR PARENT)
	DEGREE	DURATION				
12	Severe	See column 4	Resuscitated after a half hour of strenuous effort and prolonged aspiration of the bronchi	Maturity 33 weeks; total placenta previa; breech extraction, decomposition and Mauriceau maneuver; cord normal	56	59
13	Severe	Ten minutes before child breathed normally	Not indicated	Normal L.O.A.; low outlet forceps; cord normal	80	85
14	Moderate	Breathed normally after from six to seven minutes	Aspiration mucus; CO_2-O_2; Drinker respirator	Premature rupture of membranes (51 hours); maturity, 35 weeks; cord short and thick	62	129
15	Marked	No statement	Flagg and Drinker respirators; coramine adrenalin	Normal; cord normal	101	124
16	Marked	Difficulty in resuscitating infant	Aspiration of mucus; artificial respiration	Face presentation; cord normal	74	76
17	Severe	No statement	Aspiration of mucus; artificial respiration	Persistent R.O.P.; first stage, 47¾ hours; cord normal; forceps rotation	111	126
18	Fourth degree	See column 4	Flagg apparatus for thirty minutes followed by artificial respiration and CO_2-O_2 for five minutes	Persistent R.O.P.; forceps rotation; Scanzoni, Piper outlet; cord normal	87	90
19	Severe	See column 5	Not indicated	Dry labor six hours, fifteen minutes; fetal heart sounds variable in rate on day preceding birth; thick green amniotic fluid; cord not pulsating at birth	119	101

TABLE II

COMPARISON OF INTELLIGENCE QUOTIENTS

GROUP A		
CASE	ASPHYXIATED	CONTROL
1	48	95
2	52	70
3	76	101
4	118	132
5	98	104
6	77	78
7	112	102
8	104	110
9	93	107
10	92	94
Mean	87	99.3

GROUP B		
CASE	ASPHYXIATED	CONTROL
11	113	126
12	56	59
13	80	85
14	62	129
Mean	77.7	99.7

GROUP C		
CASE	ASPHYXIATED	CONTROL
15	101	124
16	74	76
17	111	126
18	87	90
19	119	101
Mean	98.4	103.4

orrhage had not been diagnosed. The presence of crenated red blood cells and a positive benzidine test of the cerebrospinal fluid give the best evidence of intracranial hemorrhage. However, Capper[2] states that 10 per cent of all newborn infants may show red blood cells in the cerebrospinal fluid, although they show no signs of cerebral hemorrhage and later develop no residual symptoms. Clear cerebrospinal fluid has been obtained from infants who were later proved to have cerebral hemorrhage.

Research work endeavoring to study the relationship between various traumatic factors at the time of birth and subsequent mental development has been handicapped until recently by the lack of one mental scale that could be used in children of both preschool and school age. Consequently, clinical impression, school achievement or grade level, and parental reports have been the unsatisfactory foundation upon which all of the early research and much of the more recent research work related to mental development has been based. The 1937 revision of the Stanford-Binet Intelligence Scale[30] requires individual administration, and hence more time, but affords a reliable and valid measurement of intelligence from the 2-year level through adult life. This scale was administered by the same examiner for all subjects considered in this study. Correction for the amount of prematurity was made in the calculation of the chronological age for the few infants born prematurely (Table I).

Because of genetic factors and environmental factors operating in the determination of intelligence, it was thought advisable to use the parents or preferably the siblings of the asphyxiated children for the control group. By this method a control group correlating as highly as possible (with the exception of twin controls) in mental ability is secured. The correlation between the intelligence of parents and their children in the general population is reported to range from .45 to .55.[16, p. 716] The

coefficient of correlation between the intelligence of siblings on the Stanford-Binet scale in the general population is reported to range from .40 to .68.[22, p. 512]

FINDINGS AND METHOD OF PRESENT STUDY

The statistical method of analysis consists of the use of Student's T-test[27] for unique samples to determine whether there is a significant mean difference between subjects in the asphyxiated and control groups.

It was found that the children in the asphyxiated group had a mean I.Q. of 88.05 while those in the control group had a mean I.Q. of 100.47. In Fig. 1 is shown the relationship between the I.Q.'s of the subjects in each group. Of nineteen severely asphyxiated children studied, only

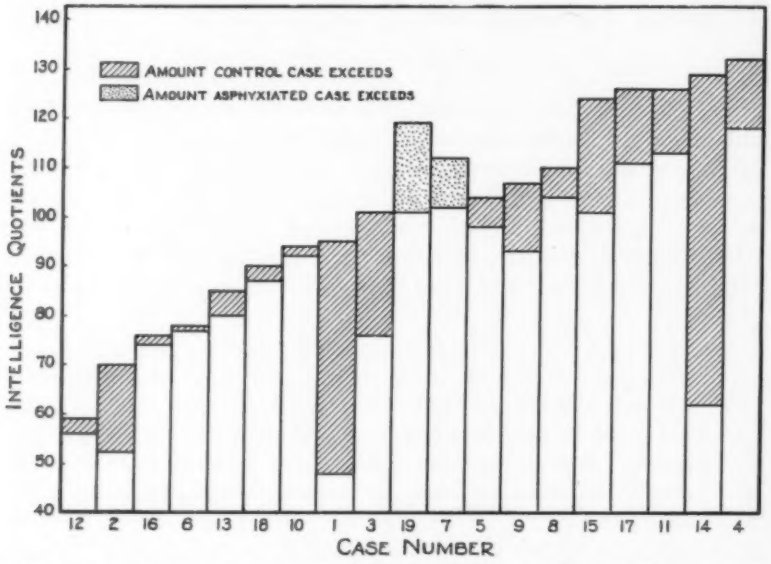

Fig. 1.—Graphic comparison of intelligence quotients of children studied. Control cases are arbitrarily arranged in order of ascending intelligence quotients.

two (cases 7 and 19) showed a higher intelligence quotient than the corresponding members in the control group. The child in Case 7 (Table I) may or may not have been a case of asphyxia pallida as judged. The child in Case 19 (Table I) was included because of "severe" degree as indicated on the hospital record and the lack of cord pulsation at birth.

For the determination of the presence or absence of a statistically significant difference, the I.Q.'s were changed to standard scores which afford a more reliable figure for use in statistical evaluation. The mean standard score of the total number of subjects in the asphyxiated group was –.747, while the mean of the total number in the control group was plus .03. The mean difference ($\bar{x}$) of –.777 is found to be highly sig-

nificant by using Student's T-test for unique samples. Standard error ($S_{\bar{x}}$) = .23

$$t = \frac{\bar{x} - m}{S_{\bar{x}}} = 3.37$$

3.37 exceeds 2.878 at 18 degrees of freedom in Fisher's table[13, p. 177] for the value of t. The difference is, therefore, highly significant of a difference between the means of the two groups. The value of P is .01 or less. (Less than or equal to one chance in one hundred of being pure chance.)

The significance of the mean difference between those asphyxiated infants included in Group A and their controls was also determined. The mean standard score of those in the asphyxiated group (Group A) was –.813, while the mean of the control group (A) was –.042. The mean difference ($\bar{x}$) of –.771 is found to be highly significant. t equals 2.91 and exceeds 2.821 at 9 degrees of freedom in Fisher's table of t values. P, therefore, equals .02 or less.

The significance of the mean difference between those in the combined groups, A and B, and their controls was determined. The mean standard score of the asphyxiated children (A + B) was –1.369, while the mean of the control subjects (A + B) was –.048. The mean difference of –1.321 is found to be highly significant. t equals 4.26, and exceeds 3.012 at 13 degrees of freedom in Fisher's table of the value of t, which makes P equal to .01 or less.

DISCUSSION

It is, therefore, shown that a statistically significant difference in mental status exists between a group of children severely asphyxiated and apneic at birth and a control group consisting of their siblings or parents. This is shown for the total group and also for subdivisions of the total group.

The far reaching implications of this finding are at once apparent. The reduction and treatment of cases of anoxia at birth offer a point of attack at which some hope for the reduction of the number of mental defective individuals may be had. The preventive and therapeutic methods by which this reduction of anoxia in the newborn infant is to be attained are outside the scope of the present paper.

With mental retardation likely in very severely asphyxiated children and a possibility in asphyxiated children, the importance of using oxygen therapy for all asphyxiated children may again be emphasized. From a preventive aspect, the recent use[13] of continuous caudal anesthesia in obstetrics with its apparent reduction of delivery trauma, elimination of narcosis, and shortening of the second stage of labor may prove to be of value.

The study of the mental development of children in whom umbilical vein blood oxygen and lactic acid content is known[9, 10] should be of interest in determining more definitely the degree of anoxemia resulting

in mental retardation. There is apparently a combination of degree and duration of anoxia from which nervous tissues are unable to recover adequately. Less severely asphyxiated children[19] do not appear to be significantly retarded in mental development.

CONCLUSION

Very severely asphyxiated and apneic newborn infants, with no physical evidence of injury at birth or following, are significantly retarded in mental development.

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THE EFFECT OF VITAMIN D FROM COD-LIVER OIL AND A TUNA-LIVER OIL UPON SERUM PHOSPHATASE CONCENTRATIONS IN RACHITIC INFANTS

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IN RECENT years the dual assay method,[1] using rats and chicks for distinguishing between the various forms of vitamin D found in liver oils of different species of fish, has become the usual procedure. Using this technique, Bills, Massengale, Imboden and Hall[2] reported assays on liver oils from twenty-five species of fish. They found that rat unit for rat unit the oils differed widely in their relative effectiveness on chicks as measured by the ash content of the femurs. Correll and Wise,[3, 4] found a variation in the response of chicks to certain tuna-liver oils when fed at equal rat unit levels, as measured by bone ash, growth, and serum phosphatase.

Bills and co-workers[2] suggested that the different biologic responses obtained with chickens when compared with rats might be due to the existence of vitamin D in several different chemical forms in a single oil, some chemical entities for a particular specie being more efficient than others.

It has been reported by Barnes and Carpenter[5] that serum phosphatase values in otherwise normal infants serve as a sound basis for the clinical diagnosis and prognosis of rickets. We were interested, therefore, to ascertain how cod-liver oil and a tuna-liver oil (known to be less efficient than cod-liver oil on chicks) would compare as to their effect on the magnitude and rate of reduction of serum phosphatase when administered to rachitic infants at equal rat unit dosages (600, 900, and 2,400 I. U. daily). The purpose of this paper is to report data on forty-eight rachitic infants subjected to such a study.

CLINICAL PROCEDURE

Seven hundred and ninety-eight infants were examined for study. They came from the Child Welfare Clinic, Detroit Department of Public Health, and were considered possibly rachitic on the basis of a history of low or no vitamin D intake and the obvious presence of two or more commonly accepted physical signs of rickets (head sweats, Harrison's groove, rachitic rosary, widened epiphyses, protruding frontal bosses, and craniotabies). One hundred and eighty-nine of these infants had a serum phosphatase of 20 units or more, which was considered sufficiently above the normal phosphatase value[6] to be indicative of rickets. Case selection was on the basis of serum phosphatase. The use of serum

From Harper Hospital.

phosphatase in the diagnosis and treatment of rickets as compared with x-ray or serum calcium and phosphorus has been discussed in a previous paper.[5] All 189 infants were placed on treatment. Thirty-seven were treated in the metabolic ward and the cases of these infants will be presented in a future paper. The rachitic infants were so divided that each medication was tested on approximately the same number of infants, who were matched as to phosphatase levels, thereby presenting as nearly as possible a similar range of initial serum phosphatase for each group. Treatment of some of the patients was discontinued after a few weeks because of acute infections or lack of parental cooperation. A study of forty-eight infants is reported in this paper.

This was an outpatient study. Careful follow-up and checking in the home was done twice a week by a competent nurse familiar with the work who devoted her time exclusively to this problem. Emphasis was placed on the importance of proper dosage and regular feeding of vitamin D, orange juice, milk, and iron, if prescribed. Patients were continued on treatment and retained in the experiment only when the mothers cooperated well. In addition to vitamin D, the furnishing of a quart of fresh milk and oranges to all assured an adequate supply of calcium, phosphorus, and vitamin C for the infants. The mothers of breast-fed babies were instructed to drink the milk which was provided for them. If the patients had a hemoglobin of 10 Gm. (Hayden, Hauser) or less per 100 c.c. of whole blood, an iron and liver preparation was provided.

These data were accumulated during the months from November to June, 1933-1934, 1934-1935, 1936-1937, 1937-1938, and 1938-1939. From

TABLE I

VITAMIN D SUPPLEMENT, TYPE OF MILK, NUMBER OF LOW CALCIUM AND PHOSPHORUS VALUES, INITIAL X-RAY READINGS

VITAMIN D (I.U.)	INFANTS TREATED	BREAST FED		FORMULA OR WHOLE MILK		INITIAL CA BELOW 10.4 MG. PER 100 C.C. SERUM	INITIAL P BELOW 5.5 MG. PER 100 C.C. SERUM	INITIAL X-RAY READINGS‡				
		N*	W†	N	W			A	B	C	D	E
Cod-liver oil												
600	10	5	1	4		2	4	3	1			3
900	7	4		3		6	8	6	1			
2,400	7	1		4	1	6	7	6				
Tuna-liver oil												
600	10	4	3	3		2	7	1	2			4
900	7	3		3	1	2	6	4	1			1
2,400	7	3		2	2		4	3	1			3
Totals	48	20	4	19	4	18	36	23	6			11

*N, Negro infants.

†W, White infants.

‡Initial x-rays were not obtained on eight infants.

X-ray readings: A, Active rickets; B, healing rickets; C, Cured rickets; D, doubtful rickets; E, Normal.

November to June is the period of least sunshine and the greatest occurrence of rickets. The patients were brought to the clinic once a week during the first two weeks of treatment, then once every two weeks thereafter. The data presented in this paper cover the first six weeks of treatment, although many of the cases were studied for a much longer time. Blood specimens were obtained from the femoral vein for serum calcium,[7] phosphorus, and phosphatase.[8, 9] The bones of the wrists were x-rayed every two weeks. Complete blood counts were taken regularly. A weight record was kept of each patient and dietary changes made to insure adequate diet as the baby grew. The age of the patients ranged from 1 month to 1 year and 6 months. Eight babies were white and thirty-nine were Negro. Four white infants and 20 Negro infants were breast fed during all or part of the study (Table I).

Cod-liver oil concentrate and a tuna-liver oil (H tuna) were used as the source of vitamin D supplements. Both oils had been previously assayed on the rat and chick.* The cod-liver oil concentrate was equally efficient for chicks (efficacy ratio = 100 per cent) when compared with a reference cod-liver oil rat unit for rat unit, while the tuna-liver oil was found to be only 62 per cent as effective as the vitamin D of cod-liver oil when fed at equal rat unit levels.

Each of the vitamin D preparations was fed to the infants in concentrations of 600, 900, and 2,400 I.U. per day. The vitamin D concentrates were diluted so that 20 drops was the daily dose. This amount was dropped by means of a calibrated dropper into the infant's mouth and was followed immediately by orange juice.

RESULTS AND STATISTICAL ANALYSIS

In order to compare the effect of vitamin D from cod-liver oil and the tuna-liver oil upon the elevated serum phosphatase, it was thought best to select cases which would yield an initial common average phosphatase value for each group within three days prior to medication. This necessitated the exclusion of many cases studied. The forty-eight infants whose cases are recorded here all had an initial serum phosphatase of 20 units or more; the average initial value for each group was from 27 to 28 units per 100 c.c. of serum. Of the forty-eight cases

*Assayed in the laboratories of The Upjohn Co. Protocol submitted to the authors is as follows:

RESPONSE OBTAINED AFTER FEEDING CHICKS FOR THEIR FIRST TWENTY-ONE DAYS, DIETS CONTAINING 18 I. U. OF VITAMIN D FROM THE SOURCES INDICATED

SOURCE OF VITAMIN D	TIBIA ASH (%)	I. U. INDICATED BY BONE ASH ON BASIS C.L.O.-100	EFFICACY RATIO (%)	PHOSPHATASE PER 100 C.C. SERUM (UNITS)
Cod-liver oil (Reference standard)	44.4	18	100	50
Cod-liver oil (Concentrate)	45.0	18+	100	50.4
H Tuna-liver oil	39.7	11.2	62	70.0

H Tuna-Liver Oil is Tuna Liver Oil No. 3 in the publications of Correll and Wise.[3, 4]

in Table I, 37 per cent of the infants had a serum calcium below 10.4 mg., while 75 per cent had an initial serum phosphorus below 5.5 mg. per 100 c.c., indicating that these rachitic infants had a predominately low serum phosphorus. The initial x-rays, which were taken on the same day as the first blood chemistry, are recorded in Table I.

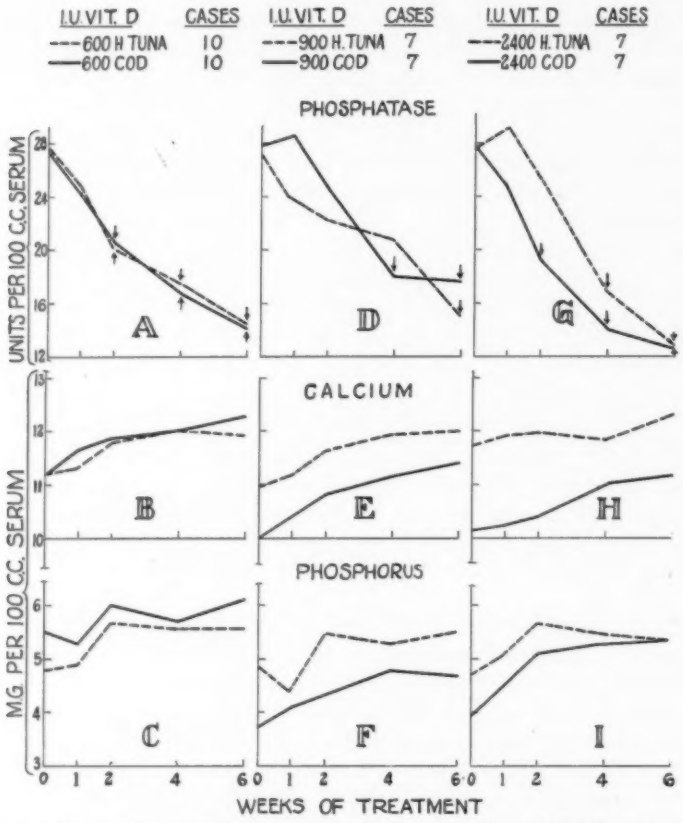

Fig. 1.—Effect of vitamin D from cod-liver oil and a tuna-liver oil at three levels on serum phosphatase, calcium, and phosphorus values.

The serum calcium phosphorus and phosphatase of the infants in each group were averaged before medication and after the first, second, fourth, and sixth week of treatment. The average effect on these serum constituents from medication over a period of six weeks with cod-liver oil at three different levels (600, 900, and 2,400 I.U.) as compared with H tuna, level for level, is presented in Fig. 1. After the first week all medications caused a continued serum phosphatase decline and an increase in serum calcium and phosphorus above the initial value.

The phosphatase data obtained were treated statistically according to two formulas based on Fisher's method[10] for determining the significance of means of small samples. The first statistical approach was by comparison of means* in which the mean phosphatase value for one

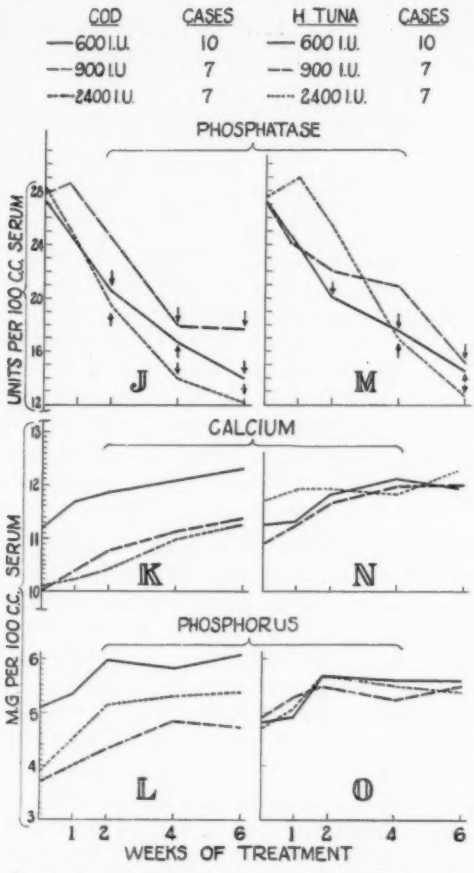

Fig. 2.—Effect of three concentrations of vitamin D from cod-liver oil and a tuna-liver oil upon average serum phosphatase, calcium, and phosphorus values.

*

$$t = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{n_1 s_1^2 + n_2 s_2^2}} \sqrt{n_1 + n_2 - 2} \sqrt{\frac{n_1 n_2}{n_1 + n_2}}$$

$\bar{x}_1$ = The mean phosphatase value for infants in Group 1.
$\bar{x}_2$ = The mean phosphatase value for infants in Group 2.
n_1 = The number of infants in Group 1.
n_2 = The number of infants in Group 2.
s_1^2 = The estimate of standard deviation for infants in Group 1.
s_2^2 = The estimate of standard deviation for infants in Group 2.

group was compared with the mean phosphatase value of another group at a certain time interval after starting vitamin D therapy. Since the average initial phosphatase values for the infants in all groups were similar, this method was considered reliable for making subsequent comparisons between the groups. In this way, the difference in magnitude of phosphatase reduction by one medication was compared with that caused by another medication at the same time interval.

No significant difference was found in the magnitude between the average serum phosphatase response curves for H tuna and cod-liver oil when fed at the same level of 600, 900 and 2,400 I.U. per day over a period of six weeks (Fig. 1, *A*, *D*, and *G*). Likewise these three different concentrations of the same fish liver oil, although producing slightly different average phosphatase curves, did not demonstrate according to this same statistical study any significant difference in the magnitude of serum phosphatase reduction during the first six weeks of medication (Fig. 2, *J* and *M*). Therefore, while for each oil the average serum phosphatase actually more nearly approaches a normal level when the highest (2,400 I.U.) daily dose is given for six weeks, the differences when compared in this manner with the other two levels (600 and 900 I.U.) are not significant. Thus, at these dosages there appears to be no direct relationship between vitamin D intake and phosphatase reduction.

The second statistical approach was by "pairing," that is, taking the initial phosphatase value for each child and the phosphatase value for that child after vitamin D administration was started. By combining these differences for each group of patients at one-week, etc., intervals, "t" values* were obtained, some of which were considered significant; that is, having a probability of not more than five times in a hundred, according to Fisher's tables of "t" values. This method showed the "rate" at which significant phosphatase reduction occurred in the infants in each group. Significant rates of phosphatase reduction are indicated by arrows on the average curves (Fig. 1, *A*, *D*, and *G*). The rate of serum phosphatase (see arrows) was statistically significant in all infants by the sixth week of treatment; this is also true even at the fourth week of treatment, with the possible exception of the group in which the infants received 900 I.U. of H tuna.

*

$$t = \frac{\bar{x}\sqrt{n-1}}{\sqrt{s_x}} = \frac{\bar{x}\sqrt{n-1}}{\sqrt{\frac{S(x^2) - \bar{x}^2}{n}}}$$

x = The difference between the phosphatase value before vitamin D therapy and the phosphatase value at a later time interval during the vitamin D therapy.
$\bar{x}$ = The mean difference for the infants in the group.
n = The number of infants.
s_x = The standard deviation for the infants in the group.
$S(x^2)$ = The summation of the squares of the x's.

COMMENTS

Biologic experiments, particularly using the chick, have repeatedly demonstrated that some fish liver oils are less efficient as antirachitic agents than cod-liver oil when fed at equal rat unit levels. This has been offered as evidence that vitamin D exists in these oils in several chemical forms which give varying responses in different species. Bills, Massengale, Imboden, and Hall[2] report some tuna-liver oils to have an antirachitic effectiveness on chicks, when compared with cod-liver oil, of only 16 per cent and lower, while a yellow fin tuna-liver oil was 136 per cent as effective.

We had for clinical investigation a tuna-liver oil which assayed on chicks, as measured by bone ash and serum phosphatase determinations, only 62 per cent the effectiveness of cod-liver oil when fed at equal rat unit levels.

Under the conditions of this investigation, no significant difference was found, as measured by serum phosphatase concentrations, in the response of rachitic infants to either the cod-liver oil or the tuna-liver oil at any of the three rat unit levels studied (600, 900, and 2,400 I.U.). This would indicate that in human beings there is no specie preference for the vitamin D from cod-liver oil and this particular tuna-liver oil at the dosage levels fed. Whether a fish liver oil with a much lower efficiency ratio, as measured on chicks, would be less effective clinically is an unanswered question. There also remains the question of what responses would be obtained clinically if the oils were compared at lower, borderline doses.

Likewise, the data presented here indicate that within the same oil the physiologic response was practically the same at dosages of 600, 900, or 2,400 I.U. daily. With both cod-liver oil and the tuna-liver oil and at all three levels, it was found that serum phosphatase concentrations were significantly lowered, approaching normal values, by the sixth week of medication. Actually, in nearly every infant the "rate" of phosphatase reduction was significant by the fourth week. Using serum phosphatase responses as a criterion, this work would indicate that for most infants with clinical rickets, daily administration of 600 I.U. of vitamin D from cod-liver oil and some tuna-liver oils should be ample as a curative dose.

CONCLUSIONS

Forty-eight infants with clinical rickets, as indicated by elevated serum phosphatase concentrations, were divided into groups and treated with vitamin D from cod-liver oil and a tuna-liver oil (known to be only 62 per cent as effective as cod-liver oil on chicks) at three dosage levels (600, 900, and 2,400 I.U. daily).

No significant difference was found in the magnitude of serum phosphatase reduction by either of the oils at any level.

Both liver oils at all three medication levels demonstrated significant rates of serum phosphatase lowering by the sixth week. With only one exception, this was true by the fourth week.

When the three dose groups within the same oil were compared, no significant difference was found in their relative degree of serum phosphatase reduction during the first six weeks of treatment. All approached normal values by the sixth week.

Under the conditions of this study it is indicated that 600 I.U. of vitamin D daily from cod-liver oil or some of the tuna-liver oils are ample as a curative dose for clinical rickets.

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FURTHER OBSERVATIONS ON THE USE OF SINGLE MASSIVE DOSES OF VITAMIN D IN THE PREVENTION OF RICKETS

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THIS report concerns further observations on the use of single massive doses of vitamin D in the prevention of rickets in infants. In a previous communication a description of the treatment of sixty-two infants by this method was given. Although single massive doses of vitamin D were used experimentally in animals as early as 1928,[2] and later clinically for the treatment of rickets, it was not until 1938 that Harnapp[3] first employed this method for the prevention of rickets in infants. Since then numerous authors in Germany and elsewhere have utilized this procedure with effective results. The literature on the subject has been previously reviewed[1] and may be summarized as follows:

1. *Advantages of Massive Dose Vitamin D Prophylaxis of Rickets.*—The massive dose method is timesaving. Only two oral doses are necessary during the winter and spring months, instead of the orthodox daily doses. Objections to oily preparations are avoided by mother and baby. The method is of advantage in allergic infants in whom regurgitation of feedings occurs. The method is inexpensive. It is of value where the daily dose method is not faithfully carried out.

2. *Rationale of Massive Dose Method.*—There is experimental as well as clinical evidence to show that vitamin D is absorbed unchanged and that it circulates in the blood stream; that it is stored in various tissues without inactivation; that it may be metabolized and excreted in amounts depending on the dose administered; and that it is better absorbed and stored if the dose is massive.

In laboratory animals, Heymann,[4] in 1936, found detectable amounts of vitamin D circulating in the blood from two to three months after the administration of a single oral dose of 200,000 units of vitamin D. The vitamin was stored in the brain, erythrocytes, lungs, kidneys, liver, and blood plasma in ascending order of effectiveness. In adult human beings Warkany[5] found that after abrupt withdrawal of high daily doses of vitamin D, from three to six months elapsed before the concentration of vitamin D in the blood serum fell to a normal level.

3. *Safety of Single Massive Doses of Vitamin D.*—The margin of safety in administering large doses of vitamin D is very great, and no fear need be entertained in its use unless toxic levels are maintained for a period of time. The early literature on the toxicity of vitamin D

From the Matlock Street Well-Baby Station, Board of Health; Dr. Frederick Lee, Health Officer.

U. S. P. units referred to throughout.

has to be discarded because impure preparations containing toxisterols were used, and these early preparations were not standardized as to potency of vitamin D.[6] In the rat, Bills and Wirick[7] in long-time feeding experiments have shown that a dosage of 1,000 times that of the minimum rachitic level was just perceptibly harmful. In short-time feeding experiments others[8] have shown that between 5,000 and 100,000 overdosage is lethal. Steck, Deutsch, Reed, and Struck,[9] in 1937, in experiments on dogs and human subjects reported that it was important to record data as to the dose per unit of body weight. Both animals and human beings generally survive the administration of 20,000 units per kilogram per day of vitamin D for indefinite periods without intoxication. Levels beyond this are toxic. Reed, Struck, and Steck[10] have shown experimentally in dogs that even if calcification is produced in the kidneys, the process is reversible if the administration of vitamin D is stopped.

The use of large doses of purified preparations of vitamin D in infants and children has been conclusively shown to be safe in single doses or in short-time administration, except in the presence of kidney disease. In 1930 Hess, Poncher, Dale, and Klein,[11] using 600 and 1,000 D viosterol in twelve infants, six of whom were Negroes, showed that doses from twenty to fifty-two times the prophylactic dose in long-time feeding periods (six to eight months) were not toxic for these infants. They also found that infants tolerated 250 times overdosage well for short periods. No clinical symptoms of toxicity developed. Since 1936, when purer preparations of vitamin D became available, doses ranging from 200,000 to 600,000 units for the treatment and prevention of rickets have been used without any toxic effects.[12] Zelson[13] even administered 600,000 units of vitamin D orally and parenterally to forty-six premature infants between 12 and 33 days of age without toxicity.

If renal disease exists, such as chronic interstitial nephritis, polycystic kidneys, hydronephrosis, or pyelonephritis, the use of large doses of vitamin D may predispose to metastatic calcification. However, calcification of the arteries and organs in infants may result from disturbances of calcium metabolism due to factors other than vitamin D.

4. *Recommended Dosage for Single Massive Dose Vitamin D Prophylaxis.*—The work of Harnapp, Windorfer, Heisler[14] and others has shown that infants ranging in age between 2 months and 1½ years can be adequately protected against rickets for the duration of the winter with a single dose of from 400,000 to 600,000 units of vitamin D. Mild rickets may develop in a small number of infants if the dose given is lower (200,000 or 300,000 units). Therefore, if the latter dosage is used, it must be repeated a few months later. Premature infants require at least 400,000 units in a single massive dose.

In the first series of cases I reported,[1] 600,000 units of vitamin D was given in two divided consecutive doses, about the third month of life, or later. The weight of these infants varied between ten and sixteen

pounds. Vitamin D was given in the form of electrically activated ergosterol* and was well tolerated. At that time I suggested the following plan for massive dose rickets prophylaxis which I considered safe and effective: the administration of 50,000 units of vitamin D at 1 month of age and a second 50,000 units at 2 months of age, preferably in milk; then the administration of 600,000 units of vitamin D in powder form (ertron), at about the third month, in cereal. This dose may be repeated from three to six months later.

REPORT OF STUDY

This study was undertaken to determine the efficacy of single massive doses of vitamin D administered in the following manner: 50,000 units of vitamin D at the age of 1 month, 50,000 units at the age of 2 months, and then 600,000 units of vitamin D at about 3 months of age. The 50,000 units of vitamin D were administered in the form of electrically activated vitamin D suspended in corn oil, so that twelve drops contained the prescribed amount of vitamin D.† This was added directly to one bottle of the infant's formula and the mother was instructed to give the full amount. The oil was well tolerated and no regurgitation was encountered.

At or just prior to the third month, the infant was started on a precooked cereal, and usually in about one week he was taking a sufficient amount in which to mix the electrically activated ergosterol, available in powder form (ertron). Each capsule of this preparation contains 50,000 units of vitamin D. The mother was given twelve capsules (600,000 units) with printed as well as oral instructions for its administration. She was told to empty the contents of six of the capsules and mix them with one tablespoonful of precooked cereal. The warm formula was added, the mixture stirred, and fed to the baby. The second six capsules were similarly administered the following morning. The purpose of this was (1) to avoid altering the taste of the cereal, (2) in case the feeding was refused or regurgitated, only six capsules would be lost, and (3) probably better absorption with less loss of the vitamin through the bowel was possible if the activated ergosterol was given in two divided doses twenty-four hours apart. Precooked cereal is well suited for the administration of this preparation of activated ergosterol.

The study was begun in September, 1942, and was concluded the first week of June, 1943. Most of the babies studied were seen in private practice and the rest were seen at the Matlock Street Well-Baby Station of the Paterson Board of Health, Paterson, N. J. The infants were examined clinically for rickets (beading, craniotabes, knobbing of wrists,

*Ertron, Nutrition Research Laboratories, Chicago, Ill. In the manufacture of Ertron, ergosterol is first heated in a partial vacuum until it is vaporized. While it is in a gaseous state, an electric current of controlled amperage and voltage is passed through it, and kept there for a definite length of time. It is then bio-assayed according to the U.S.P. method for vitamin D and diluted in a solid fat and other inert material.

†Prepared for the purpose of this study by the Nutrition Research Laboratories, Chicago, Ill.

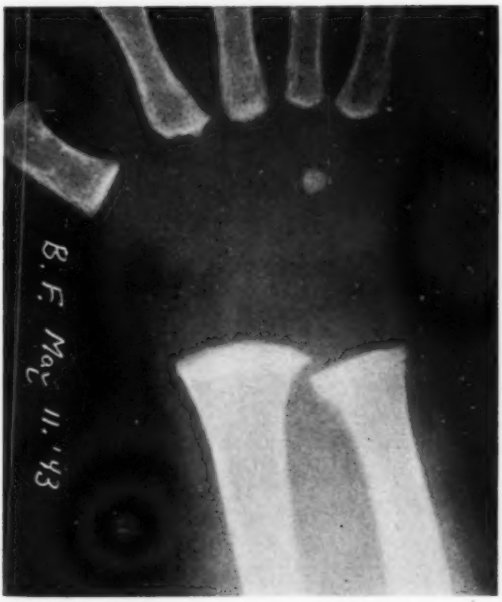
A.

B.

Fig. 1.—Infant B. S. *A*, Age, 3 months; weight, 12 pounds, 14 ounces; breast-fed. At 1 and 2 months of age, respectively, he received 50,000 units of vitamin D orally. One month later, Jan. 6, 1943, at the age of 3 months, a roentgenogram showed very mild rickets. A dose of 600,000 units of vitamin D was given in two divided doses.

B, May 11, 1943, four months and five days after the massive dose of vitamin D; rickets healed and no recurrence without further vitamin D.

A.



B.

Fig. 2.—Infant B. F. *A*, Age, 3 months; weight, 13 pounds, 4 ounces. Received irradiated evaporated milk for three weeks, then 50,000 units of vitamin D at 1 and 2 months of age, respectively. Roentgenogram Jan. 6, 1943, at the age of 3 months showed mild rickets. Given 600,000 units vitamin D in two divided doses.

B, May 11, 1943, four months and five days after massive dose of vitamin D; rickets healed and no recurrence without further dosage.

and Harrison's groove) once a month. An x-ray film of the right wrist was taken at the third month prior to the administration of the 600,000 units of vitamin D and again at the conclusion of the follow-up of each infant. All films were taken by Dr. J. Roemer.* The films were reviewed by both of us at the end of the study. An attempt was made to accept only those babies who had had no previous form of vitamin D, but this was not entirely possible due to the widespread use of irradiated evaporated milk. About one-half the infants followed were on irradiated milk for a period of from one to four weeks at the time of instituting the study. Thereafter the infants remained on a vitamin D-free milk, and no egg yolk was given until the study was concluded in each instance.

New foods were introduced into the diet as follows: precooked cereals about the third month; banana and strained vegetables at the fourth month; soups and stewed fruits about the fifth month; puddings about the eighth month. No vitamin A was given except that available in natural form in the milk.

Fifty infants were enrolled in this study, but due to war conditions it was possible to follow only twenty-one. All the infants studied were white. Five were breast fed for variable periods of time. Two of these twenty-one infants showed slight rickets at the ulnar metaphysis when x-ray films were taken at the age of 3 months. In both instances, four months and five days after 600,000 units of vitamin D had been given, a second x-ray film of the metaphyses showed that the rickets had healed and remained normal (Figs. 1 and 2). In the remaining nineteen patients, the metaphyses were normal at the time of first roentgen examination at from 3 to 6 months of age and remained normal for periods

TABLE I

FOLLOW-UP PERIOD

ON 600,000 UNITS OF VITAMIN D

MONTHS	NUMBER OF CASES
2 to 3	3
3 to 4	8
4 to 5	5
5 to 6	5
Total	21

TABLE II

TOTAL FOLLOW-UP PERIOD

MONTHS	NUMBER OF CASES
4 to 5	2
5 to 6	7
6 to 7	8
7 to 8	3
8 to 9	1
Total	21

*Roentgenograms were taken by Dr. Jacob Roemer, Chief Roentgenologist, Barnert Memorial Hospital, Paterson, N. J.

of from two months and nine days to six months (Table I). The twenty-one patients were followed for a total period of from four to nine months (Table II).

COMMENT

The single massive doses of vitamin D given at the ages of 1, 2, and 3 months or older, respectively, were well tolerated and produced no ill effects. A repeat dose of 600,000 units was given from four to five months after its first administration. Two of these twenty-one infants showed minimal signs of rickets on x-ray examination one month after a second single massive dose of 50,000 units of vitamin D. However, in both infants, four months after 600,000 units of vitamin D had been given, the process was fully healed. In a previous study[1] fourteen infants between the ages of 3 and 5 months were found to have slight rickets and four were found to have more marked rickets on x-ray examination of the ulnar metaphyses at the onset of the study. Four of these infants previously studied were breast fed for one month or longer but received no form of antirachitic agent. Three others had been on irradiated evaporated milk for about one month, and the remaining eleven infants in this group of eighteen mildly rachitic infants were on irradiated evaporated milk and average prophylactic doses (1,000 I. U.) of 50 per cent percomorphum oil or viosterol for one month or more prior to receiving a massive dose of vitamin D.

Rhoads, Rapoport, Kennedy and Stokes[15] found a total incidence of rickets in one of their studies on the prevention of rickets to be 13.7 per cent in infants receiving between 110 and 1,500 units of vitamin D daily. On the other hand, they included, in their normal group, infants who showed bone changes which they considered nonrachitic, although they observed cupping and so forth in this group. These so-called nonrachitic changes occurred in about 40 to 50 per cent of the infants observed. These authors quoted Eliot and her coworkers in Detroit who, using from 135 to 735 units of vitamin D in the form of various antirachitic agents, found rickets exclusive of doubtful rickets in 36 per cent white males and 28 per cent colored males. Roddy and his coworkers[16] in Philadelphia, found 25 per cent rickets occurring in eighty-four initially nonrachitic infants followed for four and one-half months on 2,140 or 1,070 units of vitamin D in the form of percomorph-liver oil. Rhoads and his associates state a certain amount of clinically insignificant rickets is bound to occur with usual doses of customary antirachitic agents.

In view of these data then, the fact that we found two out of twenty-one infants with slight rachitic changes at the ulnar metaphyses after two single massive doses of 50,000 units of vitamin D does not vitiate the effectiveness of the method. The administration of 600,000 units brings about prompt and permanent healing.

The ten infants who received irradiated evaporated milk for a period of from one to four weeks prior to the onset of this study have been included because vitamin D is poorly stored unless given in massive doses and, therefore, obviates this objection. Breast-fed infants were also included because it has been shown that vitamin D is not secreted by the breast. No additional vitamin A was administered to the infants in this study or in the previous one because vitamin A is found in adequate amounts in cow's milk and evaporated milk. If the evaporated milk is irradiated, the loss of vitamin A is reduced to a minimum if the vitamin A inactivating ozone is removed by ventilators from the irradiating machine.[17] No evidence of vitamin A deficiency was seen.

Although the administration of 600,000 units of vitamin D in a single or divided dose is perfectly safe even for very small infants, the proposed plan in this study was to administer 50,000 units at 1 month of age and a second 50,000 units at 2 months of age, and then 600,000 units at 3 months of age. This plan precluded even the slightest possibility of vitamin D overdosage. A repeat dose of 600,000 units may be given from three to six months later, depending on the age of the infant, the season, and the clinical or roentgen findings. For example, during the summer months, the repeat dosage may be deferred until the onset of winter if the infant is older and gets plenty of sunshine. Ordinarily one should plan to administer 600,000 units of vitamin D every four months. Preschool children may be given 600,000 units of vitamin D twice a year.

A note of caution should be mentioned in attempting to diagnose mild forms of rickets clinically. It has been pointed out by numerous workers that the clinical method is wholly unreliable in mild cases. One has to depend on roentgenograms of the growing ends of the bones, particularly the ulna and radius. I mention this so that if one detects mild beading or craniotabes, one should not incriminate the massive dose method, unless rickets is diagnosed by means of an x-ray examination of the wrist. Even the development of funnelling or flaring of the ribs cannot always be attributed to rickets. Funnelling frequently develops in infants who suffer from congenital laryngeal stridor, which causes varying degrees of upper respiratory obstruction. This form of stridor may also cause mild Harrison flaring of the chest wall. Infants with large abdomens often develop flaring of the lower ribs which is nonrachitic. In rare instances muscular dystrophy may be the cause of funnelling or flaring. In this study five infants showed craniotabes either at the onset of the study or during observation. In no instance did a roentgenogram of the wrists reveal rickets at the time the x-ray picture was taken.

SUMMARY

Study of a second series of infants on single massive doses of vitamin D for the prevention of rickets again shows the effectiveness of this method of prophylaxis. The plan of administration followed was to

give 50,000 units of vitamin D at 1 month of age, 50,000 units at 2 months, and 600,000 units at 3 months of age. The 50,000 units were administered in liquid form in the formula and the 600,000 units were given in powder form (ertron) in cereal. Both dosages were well tolerated. Although it has been shown that 600,000 units of vitamin D may be given safely to very young infants, even premature ones, the method of dosage followed in this work precludes even the slightest possibility of vitamin D overdosage.

Due to war conditions it was possible to follow only twenty-one out of fifty infants originally enrolled in the study. Two of these infants showed slight rachitic changes at the ulnar metaphysis on roentgenogram one month after a second dose of 50,000 units of vitamin D. At this point 600,000 units of vitamin D was administered and in each case the rachitic process on roentgenogram was found to be healed four months and five days later. The remaining nineteen infants showed no rickets on first x-ray picture and remained protected on the dosage outlined for a total observation period of from four to nine months.

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COMPARATIVE TOXICITIES OF SULFADIAZINE AND SULFATHIAZOLE IN CHILDREN

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WHILE there is some evidence that sulfadiazine is less toxic than sulfathiazole for adults, little if any proof is to be found in the literature that the same is true of infants and children. Although a number of reports on the toxic reaction in children to one or another of the sulfonamide drugs is available, it is difficult to determine from them the relative frequency and severity of reactions and, therefore, to compare one drug with another. For these reasons we have collected and analyzed the data in two approximately equal groups of infants and children, one treated with sulfadiazine and one with sulfathiazole, observed more or less concurrently in the children's wards of the Stanford University Hospitals.

Herlitz,[1] in studying sulfathiazole toxicity in children with respiratory infections, found granulocytopenia in 4 per cent of them. By bone marrow biopsy in three children he demonstrated a definite block in maturation of granulocytes. In the same study he showed that bone marrow damage and granulocytopenia can occur, without any accompanying infection, from sulfathiazole. Finland and his associates,[2] studying 460 patients of all ages, reported a granulocyte count below 4,000 in only three patients (0.7 per cent). Flippin and his associates,[3] reporting the treatment of pneumonia in adults with sulfathiazole and sulfadiazine, found a 2 per cent incidence of granulocytopenia (below 5,000) with each drug. Satterthwaite and his associates,[4] using sulfadiazine for the treatment of urinary tract infections in adults, encountered leucopenia in 1.8 per cent. Dowling and his associates,[5] studying sulfadiazine in the treatment of pneumonia in adults, found an incidence of leucopenia (below 3,500) of 3.5 per cent. Other authors,[6, 7, 8] report similar results. Fischer and Agerty,[9] in a small series of children, found no granulocytopenias with sulfathiazole therapy.

The period of study in our cases was from June, 1941, to February, 1943, inclusive. Sulfathiazole was used throughout this period; sulfadiazine was used after September, 1941. Strict alternation of cases was not attempted. Coincident administration of alkalizing drugs was practiced intermittently throughout and fairly regularly after May, 1942. Fifty-four patients received sulfadiazine, and fifty-three received sulfathiazole. A total of 131 courses was given, the drugs being repeated in several patients. The average dose per kilogram per day was .141 Gm. for sulfadiazine and .125 Gm. for sulfathiazole. The daily

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sulfadiazine dose ranged from .04 to .27 Gm. per kilogram. The daily dose of sulfathiazole varied from .01 to .23 Gm. per kilogram. The majority of the doses from both drugs were in the .14 to .17 Gm. interval. The ages of the patients ranged from early infancy to 14 years. About 50 per cent of the children were under 2 years of age.

TABLE I

	SULFADIAZINE	SULFATHIAZOLE
Patients treated	54	53
Courses of treatment	62	69
Average days of treatment	7.0	7.0
Average total dose per kilogram	0.99 Gm.	0.94 Gm.
Average dose per kilogram a day	0.141 Gm.	0.125 Gm.
Average age of patients	2.9 yr.	3.2 yr.
Alkali* given	41 (76%)	32 (60%)
Alkali not given	13	21

*Sodium citrate or bicarbonate in amounts approximately equal to sulfonamide dosage.

Daily complete blood counts and urinalyses were done on practically all of the patients while they were receiving the drugs. Sulfonamide blood levels were determined in a few instances. Seven of the patients receiving sulfathiazole and eighteen of those receiving sulfadiazine were given concurrent .5 Gm. doses of ascorbic acid orally.

The diseases treated represent the ordinary run of acute infections seen on a pediatrics service. These are summarized in Table II.

TABLE II

DISEASES TREATED

	SULFADIAZINE	SULFATHIAZOLE
Pneumonia, uncomplicated	17	10
Pneumonia, complicated	8	9
Otitis media, purulent	10	8
Upper respiratory infections	3	5
Urinary tract infections	6	8
Miscellaneous infections	10	13
Total patients	54	53

The toxic reactions encountered are summarized in Table III.

TABLE III

TOXIC REACTIONS

	SULFADIAZINE		SULFATHIAZOLE	
	NO.	PER CENT	NO.	PER CENT
Granulopenia* (under 3,000)	24	44.3	20	37.8
Hematuria, gross	1	1.9	0	–
Hematuria, microscopic	1	1.9	1	1.9
Rashes	0	–	4	7.6
Toxic psychosis	1	1.9	0	–
Nausea and vomiting	1	1.9	0	–
Excessive crystalluria	0	–	1	1.9
Anuria	0	–	0	–
Total toxic cases	28	51.9	26	49.2

*No cases of malignant granulopenia.

Those patients whose total polymorphonuclear leucocyte count fell below 3,000 per cubic millimeter were considered to have granulocytopenia. Twenty-four (44.3 per cent) of the patients receiving sulfadiazine developed granulocytopenia. Twenty (37.8 per cent) of the patients receiving sulfathiazole showed a similar reaction. A division into three groups, according to the severity of the granulocytopenia, was made (Table IV). It appears that the incidence of the severer grades of granulocytopenia (2,000 or less) is somewhat higher for sulfadiazine (33.4 per cent) than for sulfathiazole (24.5 per cent).

TABLE IV

GRANULOPENIA

LOWEST GRANULOCYTE COUNT	SULFADIAZINE		SULFATHIAZOLE	
	NO.	PERCENTAGE OF CASES	NO.	PERCENTAGE OF CASES
3,000-2,001	6	11.1	7	13.2
2,000-1,001	11	20.4	8	15.1
Under 1,000	7	13.0	5	9.4
Total	24	44.4	20	37.7

In our series with sulfathiazole, granulocytopenia began as early as the first day of therapy and as late as the ninth day. However, more than one-half the granulocytopenias began before the fifth day. In one instance granulocytopenia (1,700 cells) developed after only one dose (.078 Gm. per kilogram) of the drug, twenty-four hours after it was given. Our experience was approximately the same with sulfadiazine, with the exception of one patient who developed granulocytopenia eighteen days after the drug was started. Fifty per cent of the granulocytopenias developed before the fifth day. There was no evidence of correlation between the severity of the granulocytopenia and the day of its onset or dosage of either drug. In the patients getting ascorbic acid, the incidence of granulocytopenia was approximately the same as that for the entire group for both drugs. We found no evidence that ascorbic acid exerted any protective action.

Five of the patients receiving sulfathiazole who developed granulocytopenia continued to receive the drug after the onset of granulocytopenia. Four of these patients had moderately severe granulocytopenia (1,200 to 1,800 cells), but none developed malignant granulocytopenia (agranulocytosis), and in every case the granulocyte count rose to normal values while the drug was continued without diminishing the dose. Four patients received sulfadiazine throughout their granulocytopenic episodes with results similar to those mentioned previously. In the majority of patients the drugs were stopped immediately at the onset of granulocytopenia. Eight patients received sulfathiazole two or more times. Of these, three developed granulocytopenia. One patient was given sulfathiazole six times for the same disease in approximately the same dosage each time; he developed granulocytopenia only on the

third course. Another patient, given the drug twice at an interval of one year, had granulocytopenia on the second course only. The third patient had granulocytopenia on both courses. Nine patients were given sulfadiazine two or more times. Five of these developed granulocytopenia. Four had granulocytopenia on both courses; one had severe granulocytopenia (648 cells) on the second course only, being treated for the same disease both times. There were no cases of agranulocytosis or purpura hemorrhagica. Platelet counts were not taken.

Fourteen patients were given both drugs with the following results:

No granulocytopenia	6
Granulocytopenia from sulfathiazole but not from sulfadiazine	2
Granulocytopenia from sulfadiazine but not from sulfathiazole	3
Granulocytopenia from both drugs	3

Three patients had hematuria (2.8 per cent). Two of these were associated with administration of sulfadiazine, one episode being gross, the other microscopic. One patient given sulfathiazole had microscopic hematuria. Forty-one (76 per cent) of those patients receiving sulfadiazine were given sodium citrate or bicarbonate in amount approximately equal to the sulfonamide dosage. Similarly, thirty-two (60 per cent) of the patients taking sulfathiazole were given alkali. The patient with gross hematuria received no alkali; the two patients with microscopic hemtauria received alkali. There was only one patient (.9 per cent) who had excessive amounts of sulfonamide crystals in his urine. He received sulfathiazole and alkali (sodium citrate). There was no case of anuria from sulfonamide administration.

There were no rashes from sulfadiazine. Four patients (7.6 per cent) developed rashes during the course of sulfathiazole therapy. Three of these eruptions resembled erythema nodosum; the other was a toxic erythema. The eruptions disappeared within twenty-four hours after the drug was discontinued. One patient, who was given sulfathiazole six times in equal dosage, had erythema nodosum on the second course, with no eruptions from the other courses.

There was only one patient (.9 per cent) who had nausea and vomiting. This was with sulfathiazole.

One patient developed delirium under heavy dosage of sulfadiazine. The sulfadiazine blood level reached 22 mg. per cent. Symptoms disappeared when the drug was stopped.

COMMENT

With the exception of skin eruptions there was no striking difference between the two drugs in the incidence of toxic reactions, despite the prevalent opinion that sulfadiazine is much less toxic. The commonest toxic effect was a fall in the polymorphonuclear count below 3,000 cells. This occurred in about 40 per cent of the patients in each series, with no great difference between the two drugs. This frequency is about ten times that reported in any other series. Apparently this high inci-

dence of granulocytopenia cannot be attributed to high dosage. The dosages used were not excessive, and there was no relation between the height of dosage and degree or incidence of granulocytopenia. Since most of the other studies have been in adults, we suspect that granulocytopenia is a much more common toxic effect in children than in adults. We do not feel that a fall in the polymorphonuclear count below normal levels necessarily presages agranulocytosis, no cases of which were observed in our series. In those patients in whom the drug was continued despite granulocytopenia, the blood counts rose slowly to normal. Nevertheless, except in the most serious infections, we feel that the drug should be stopped when there are less than 1,000 polymorphonuclear cells per cubic millimeter.

Other authors[2, 3, 7, 8, 11] report both gross and microscopic hematuria, varying in incidence from .5 to 10 per cent with both drugs. Hematuria was found less frequently in our series than in some others. Recent studies by Curtis and Sobin,[12] Fox and his associates,[13] and Gilligan, Garb, and Plummer[14] have shown that alkalinization of the urine by the administration of sodium citrate or bicarbonate is beneficial by increasing the solubility of the sulfonamides. The low incidence of hematuria and complete absence of anuria in our patients are in harmony with their observations.

Martin, Fisher, and Thompson[15] demonstrated decreased toxicity of sulfonamides in mice fed ascorbic acid. No such effect was noted in our series, despite the administration of massive doses (500 mg.) daily.

Contrary to the conclusions of Keefer,[7] Fink and Wilson,[16] and Kato and his associates,[17] we found no definite evidence of sensitization in children by repeated administration of the same drug or by the use of both drugs on the same patient. Because of the lack of relation between the incidence of granulocytopenia and daily dosage, total dosage, and length of time of drug administration, we feel that this toxic effect is due to obscure variables. It repeatedly failed to occur in subsequent courses of treatment in the same individual.

The other toxic symptoms seemed to have approximately the same incidence in children as in adults.

SUMMARY

1. The toxic reactions observed in a group of fifty-four children treated with sulfadiazine were compared with those in a group of fifty-three children treated with sulfathiazole during approximately the same period.

2. In the first group granulocytopenia occurred in 44.3 per cent of cases; in the second, in 37.8 per cent. There were no cases of agranulocytosis, even when the drug was continued after granulocytopenia appeared.

3. Simultaneous administration of alkali was employed in the majority of instances. The only case of gross hematuria occurred in a child who

had not received alkali. No instances of anuria were observed. The use of alkali appears greatly to lessen the danger of complications in the urinary system.

4. Drug rashes occurred four times, all in children receiving sulfathiazole. Three of these resembled erythema nodosum.

5. The administration of ascorbic acid in massive dosage appeared to have no detoxifying effect for the two sulfonamides studied.

6. Our observations on children fail to reveal any striking difference in toxicity between sulfadiazine and sulfathiazole with the exception of the greater incidence of rashes with the latter.

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ADVANCES IN THE CHEMOTHERAPY OF INFLUENZAL MENINGITIS

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INFLUENZAL meningitis, which occurs mainly in early childhood, formerly had a mortality rate of from 95 to 100 per cent. The use of specific antiserum intrathecally and intravenously reduced the mortality rate only to 72 per cent.[1] Furthermore, sulfanilamide, even when combined with specific antiserum, made but little difference in the death rate. Then from 1939 to 1942 very encouraging results were achieved with sulfapyridine together with serum by Neal and co-workers[2] and others.[3, 4] Hamilton and Neff[5] and McLean, Woods, and Henderson[6] both reported single cases of influenzal meningitis in which the patients were cured with sulfapyridine alone given orally in large doses. Now, most investigators still combine serum therapy with chemotherapy in the treatment of the disease.[7]

There have been eleven patients with proved cases of influenzal meningitis at the Harlem Hospital in the past seven and one-half years (January, 1936, to June, 1943). A review and analysis of these cases are presented to show the progress made in the chemotherapy of this disease. All eleven patients were children whose ages ranged from 10 months to 4½ years. They were all treated with sulfonamides. In six patients influenzal antiserum was injected intrathecally, intravenously, or by both routes. The first six patients of the series died, while the rest were cured and showed no complications.

The last three patients were treated by the routine method established at the Harlem Hospital for meningitis cases in children.[8] As soon as the diagnosis was confirmed by spinal tap, a continuous infusion of 5 per cent glucose in physiologic saline was started. A total daily dose of 1½ gr. of sodium sulfadiazine per pound of body weight was given as a 5 per cent aqueous solution, in divided doses every four hours, following four hours after the initial dose, which was one-half of the total daily dose. Intravenous therapy was continued until definite improvement was noted, and then the drug was given orally in the same dose of sulfadiazine. After from ten to fourteen days of therapy, the dosage was reduced and then the drug discontinued. In one case the child failed to respond appreciably after forty-eight hours, so chemotherapy was supplemented with *Hemophilus influenzae* type b rabbit antiserum. The cases of these three patients are reported below.

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CASE 9.—A 2-year-old girl was brought to the hospital with a history of a cold for one week, and headache, fever, and chills for one day. She vomited once shortly before admission. Examination revealed a stuporous child with opisthotonos, nuchal rigidity, absence of all deep tendon reflexes, and positive Brudzinski and Kernig signs. Her temperature was 102° F. Spinal tap produced cloudy fluid under increased pressure which contained gram-negative bacilli, identified as *H. influenzae* on culture. Analysis of the fluid showed glucose, 20 mg. per 100 c.c., and chlorides, 625 mg. per 100 c.c. An infusion of 5 per cent glucose in physiologic saline was started shortly after admission and an initial dose of 20 gr. of sodium sulfadiazine was given intravenously. This was followed by 7½ gr. of the drug injected intravenously every four hours. The child's condition remained critical after forty-eight hours, so 50 mg. (nitrogen) of *H. influenzae* type b rabbit antiserum in 200 c.c. of normal saline were given by intravenous infusion. The following day the child was alert and responsive, and her temperature had fallen to 100.8° F. The infusion was discontinued and a transfusion of 150 c.c. of blood was given. Sulfadiazine, 7½ gr. orally every four hours, was substituted for the intravenous drug. On the fifth day a spinal tap produced clear, sterile fluid under normal pressure, with a sugar level of 53 mg. per 100 c.c.; chlorides, 660 mg. per 100 c.c.; and sulfadiazine, 3.2 mg. per 100 c.c. The blood sulfadiazine level at that time was 8.7 mg. per 100 c.c. By the seventh day of hospitalization the child had become afebrile and asymptomatic. On the eleventh day the dosage of sulfadiazine was reduced to 7½ gr. four times a day, and on the fourteenth day it was discontinued. The child was discharged cured twenty-five days after admission.

CASE 10.—A 22-month-old boy had been discharged from the hospital after recovery from pneumonia for which he had been treated with sulfadiazine for several days. He was brought back to the hospital eight hours later with a headache, stiff neck, and positive Kernig and Brudzinski signs. His temperature was 99.8° F. on admission but rose soon to 103° F. Spinal tap produced cloudy fluid under greatly increased pressure. Laboratory examination of the fluid showed a sugar level of 38 mg. per 100 c.c.; chlorides, 670 mg. per 100 c.c.; and protein, 144 mg. per 100 c.c. A test for indole was positive and culture revealed *H. influenzae*. Blood culture was negative. An intravenous infusion of 5 per cent glucose in normal saline was started shortly after admission. Eighteen grains of sodium sulfadiazine were given intravenously immediately, followed by 6 gr. every four hours. By the fourth day the child had become afebrile and asymptomatic. The sulfadiazine blood level was 3.6 mg. per 100 c.c. At that time intravenous medication was replaced by oral sulfadiazine, 6 gr. every four hours. The drug was discontinued on the tenth day. Spinal fluid on the twelfth day was clear and sterile. The fluid contained sugar 63 mg. per 100 c.c., and sulfadiazine, 6.4 mg. per 100 c.c. The child made an uneventful recovery and was sent home twenty-six days after entering the hospital.

CASE 11.—A 17-month-old boy was brought to the hospital with a five-day history of fever, vomiting, cough, and listlessness. For the past day he had had purposeless twitchings of his extremities. On admission he appeared drowsy and toxic. He exhibited opisthotonos, nuchal rigidity, and positive Kernig and Brudzinski signs. His temperature was 102.4° F. Spinal tap produced turbid fluid under increased pressure. Examination of the fluid revealed 550 cells per cubic millimeter, chiefly polymorphonuclears; sugar level, 10 mg. per 100 c.c.; chlorides, 697 mg. per 100 c.c.; and protein, 64 mg. per 100 c.c. A test for indole was positive and *H. influenzae* was found in the culture of the fluid. Shortly after admission an intravenous infusion of 5 per cent glucose in normal saline was started. Eighteen grains of sodium sulfadiazine were given intravenously, fol-

lowed by 6 gr. every four hours. The temperature became normal after twenty-four hours, and the child was so much improved that the infusion was stopped and sulfadiazine, 6 gr. orally every four hours, was substituted for the intravenous medication. By the fourth day the child was asymptomatic. Spinal tap on the ninth day produced clear sterile fluid with no cells and no indole. Chemical analysis showed sugar 47 mg. per 100 c.c.; chlorides, 715; and protein, less than 7 mg. per 100 c.c. The sulfadiazine level in the spinal fluid was 8.2 mg. per 100 c.c., and in the blood, 13.0 mg. per 100 c.c. The drug was discontinued on the eleventh day. The child made an uneventful recovery.

The therapy in all of the eleven patients and the results are summarized in Table I.

TABLE I

THERAPY AND RESULTS IN ELEVEN PATIENTS WITH INFLUENZAL MENINGITIS

CASE	AGE	CHEMOTHERAPY	SERUM THERAPY	RESULT
1	2 yr.	Sulfanilamide p.o.	Antimeningococcus serum I.Th. Anti-influenzal serum I.Th. and I.V.	Died
2	10 mo.	Neoprontosil p.o.	Anti-influenzal serum I.Th. and I.V.	Died
3	21 mo.	Neoprontosil p.o. Sulfanilamide p.o.	None	Died
4	10 mo.	None	None	Died (Diagnosis made at autopsy)
5	23 mo.	Sulfapyridine p.o.	Meningococcus antitoxin I.Th.	Died
6	3 yr.	Sulfanilamide Sulfapyridine p.o. Sodium sulfapyridine I.Th.	Anti-influenzal serum I.Th.	Died
7	4½ yr.	Sodium sulfapyridine I.V. Sulfapyridine p.o.	Anti-influenzal serum I.Th. and I.V.	Cured
8	3½ yr.	Sulfapyridine p.o. Sulfanilamide p.o.	Anti-influenzal serum I.Th. and I.V.	Cured
9	2 yr.	Sodium sulfadiazine I.V. Sulfadiazine p.o.	Anti-influenzal serum I.V.	Cured
10	22 mo.	Sodium sulfadiazine I.V. Sulfadiazine p.o.	None	Cured
11	17 mo.	Sodium sulfadiazine I.V. Sulfadiazine p.o.	None	Cured

p.o., Per os.
I.Th., Intrathecally.
I.V., Intravenously.

COMMENT

Of the seven patients treated with sulfapyridine or sulfadiazine, only two died, while the three treated with neoprontosil or sulfanilamide all died. The patient in Case 5 received meningococcus antitoxin intrathecally before *H. influenzae* was cultured in the spinal fluid and was given sulfapyridine by gavage tube preterminally. In Case 6 sulfapyridine was not given the patient until the fourteenth day of illness when it was administered orally and intrathecally (as the sodium salt), with resulting temporary improvement of the patient's condition. The two patients treated with sulfadiazine were the only ones who recovered without serum. In the case where specific serum and sulfadiazine

were given, the former was administered only intravenously. In all the other cases the patients received serum intrathecally.

SUMMARY AND CONCLUSIONS

1. Eleven cases of influenzal meningitis are presented to show the progress in the chemotherapy of this disease.

2. Before the advent of chemotherapy, the mortality rate from influenzal meningitis ranged from 95 to 100 per cent. The newer sulfonamides plus serum have apparently cut this in half. In our series of eleven patients, only six died (45.4 per cent).

3. While this series of cases is small, the results indicate that influenzal meningitis can be cured with chemotherapy and serum or with chemotherapy alone. Furthermore, sulfadiazine is a very effective, if not the most effective drug, for the treatment of this disease.

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ACRODYNIA IN A THIRTEEN-YEAR-OLD BOY

Report of a Case

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ACRODYNIA is commonly a disease of infancy and early childhood. Occasional cases have been reported in older children and even in adults. Of the twenty-nine cases seen at Vanderbilt University Hospital since 1926, twenty-three have been in children younger than 2 years and fourteen were under 1 year of age. Our series included three boys in the 10- to 15-year age group. The first patient had acrodynia at 3 years of age with a recurrence seven years later. During both attacks of the disease, and at no other time, he had convulsions of a suggestive focal nature. The second case occurred in an 11-year-old boy and was similar in many respects to the third case which is reported.

The epidemic of "acrodynie"[1, 2] among adults which occurred in Paris in 1828 was subsequently attributed to chronic arsenic poisoning[3] from the wine of that region. Sporadic adult cases of acrodynia have been reported in the United States[4] and Australia.[5] It is, however, only in the more recent French literature[6-12] that one finds a detailed and vivid account of the profound alterations in personality and the emotional vicissitudes which older patients undergo and which, in our experience, constitute as characteristic a feature of the disease complex as the more classic signs and symptoms. It is of interest that these psychic and emotional disturbances may predominate the picture and precede by weeks the appearance of more easily recognizable signs of the disease, thus rendering the condition of these patients a difficult diagnostic problem.

The French patients were from 13 to 39 years of age. All had tachycardia, hypertension (blood pressure was not reported in two of the patients), marked insomnia, severe pains, most common in the extremities, sensations of burning and itching, and the appearance, after a variable length of time, of characteristic skin lesions. Asthenia, loss of weight, and profuse sweats were of fairly common occurrence. With the exception of one fatal case and one which was not further observed, all the patients made a complete recovery in from two to seven months after the onset of the disease. The emotional disturbances which were a prominent feature in every case preceded the appearance of typical skin lesions by from one to eight weeks. They were often among the first symptoms noted and not infrequently led the patient or his family

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to seek medical attention. Imbert and Tristani[11] reported a case of acrodynia in a 39-year-old woman whose first symptoms were asthenia, a burning sensation over the whole body, and profuse sweats. At the same time her character was transformed. "Formerly spirited and well-adjusted, she presented a sort of sad indifference." She was content with nothing, ill-natured, refusing to acknowledge the evident devotion of her family. The psychic state was especially disturbed, and the doctor who had been called in alarm "could scarcely believe that the patient could live in such extremity." She was a prey to hallucinations; at other times she danced about the room, opening and closing the windows, and throwing the contents of her trunk on the floor. Most of the time she had an evening delirium with marked agitation, interspersed by groans and vague complaints. "Questioning was impossible—one could only be sure that she suffered. Without regard to the consolations which were lavished on her, she reflected a mixture of indifference to our concern and at the same time despair and anxiety." A younger woman reported by Barbier and Jarricot became somber, irritable, and spoke very little. Most often seated on the bed, dishevelled, groaning and crying, she repeated over and over in a thick voice "Ah, mon Dieu." These manifestations were suspended when attention was fixed on her. A young man seen by Imbert and Chattot[12] did not present the picture of indifference but rather a constant obsession with his illness and fear of dying. He would not tolerate any conversation which did not concern itself exclusively with his illness and was possessed by a particularly intense melancholy, begging to be cured rapidly of his distressing malady. His father attested that the patient had not slept for three months and had kept the whole family awake by his outcries and his unreasonableness.

Alteration in personality and emotional disturbances were similarly striking features of the illness in the patient seen at Vanderbilt Hospital, whose case report follows.

W. P., a 13-year-old white boy, had been well until two months prior to admission to the hospital. At this time he began to have attacks of dull, aching pain and weakness in his legs, usually occurring on exercise. During many of these attacks his legs "seemed to give way beneath him" and he fell to the ground without loss of consciousness, regaining power of locomotion in a few minutes. Later the same type of pain occurred over the lower back and spread to the thighs and legs. This pain, which was described as "deep in the bones" and "boring" in character, occurred at any time of the day or night without relation to exercise, lasted two or three hours, and was severe enough to interfere with sleep. During the month before admission he had, in addition, migratory pains in the arms, neck, and lower chest, frontal headache, generalized muscular aching with occasional sharp, shooting pains in the legs and "over his heart." A dry, rough rash appeared over the chest and back, and his hands and feet often felt cold. Although he had no fever for two weeks preceding hospitalization, he had frequent "chills" during which he shook all over, had difficulty in getting his breath, and sweated profusely. These attacks lasted about fifteen minutes, were relieved by fanning or drinking water, and occurred every hour or two shortly before admission.

He lost about thirty pounds in weight during his illness and developed gradually progressive weakness to the point where he remained in bed most of the second month. At the same time there had been a striking change in the boy's personality. Formerly active and enterprising, interested in his schoolwork, farming activities, hunting, and fishing, he had become querulous and complaining. He lay in bed and demanded constantly that his mother rub his back or fan him. Sleep was restless and disturbed and he kept the entire family awake by screaming and crying out with pain.

The family history and past history were noncontributory. The parents were elderly sharecroppers of low economic status who felt helpless and bewildered at the boy's complaints and who were themselves distraught from the entailed loss of sleep.

On examination the patient was seen to be a markedly underweight adolescent boy who appeared chronically ill, sad, and anxious and who complained bitterly of numerous pains. The temperature on admission was normal and remained so throughout the hospital stay. There was a dry, rough, sudaminal eruption over the chest and shoulders. The hands and feet felt cool and appeared slightly reddened. The blood pressure in the arms was 175/130 and in the legs, 220/160. The right kidney was easily palpable but not enlarged. The remainder of the examination revealed no significant findings.

Laboratory tests failed to throw any light on the cause of his hypertension. No evidence of nephropathy was obtained from urinalyses, urine concentration, and renal function tests. Hemograms were normal and no stippling of the red blood cells was observed. Blood chemistry studies, including nonprotein nitrogen, calcium, phosphorus, cholesterol, and glucose tolerance tests, were within normal limits. Blood serology and tuberculin tests were negative. The basal metabolic rate was plus 12. The spinal fluid at the time of admission was normal and one month after admission showed slightly increased globulin with the Pandy reagent. Roentgenograms of the skull and chest and intravenous pyelogram showed no abnormality.

In the hospital the patient continued to present many and varied complaints of severe backache, headache, and pain in the extremities, chest, and abdomen. He appeared dejected and miserable, demanded constant attention from the nursing staff and, if this were not immediately forthcoming, wept and screamed. He had repeated "smothering spells" characterized by panting respirations with shivering, chilliness, and drawn facies, accompanied by complaints of precordial oppression and chest pain and followed by drenching clammy perspiration. Writhing, moaning, and begging for help, he disturbed the entire ward. These attacks which often seemed to be precipitated by emotional factors lasted from five to ten minutes and could be terminated by diverting the boy's attention. In spite of his avowed dyspnea, he could, on command, hold his breath for one minute. In addition to these symptoms the patient frequently assumed bizarre positions in which he sat or lay with his legs completely flexed, his head resting on his knees. At these times he appeared utterly dejected. He slept poorly and restlessly. The nose and upper lip were excoriated from constant picking and he succeeded in loosening and extracting two of his permanent teeth. His pulse was rapid and labile but showed no diurnal variation. The blood pressure remained constantly elevated in the vicinity of from 160/120 to 190/140 and was not appreciably lowered during sleep or sedation. Readings taken from the onset of one of the described attacks showed a very rapid rise to 250/150 with an immediate drop back to the resting level. Response to the cold pressor test was not abnormal, and subcutaneous injection of epinephrine caused no rise in blood pressure, whereas sight of the syringe and needle had raised his systolic pressure forty points a few minutes previously. Inhalation of amyl nitrate resulted in lowering of the blood pressure to normal levels and temporary alleviation of symptoms.

The most striking feature which this patient presented was his abject misery, which was reflected in his facial expression and posture. He was preoccupied with his complaints and indifferent to his surroundings. He was unable to localize his suffering well as evidenced by the migratory nature of his pains and, on questioning, stated that he "hurt all over." His suffering, however real, was somewhat minimized by his easy distractibility. So desirous was he of attention that he asked for repeated lumbar punctures, saying that he felt better "when the pus was drawn off his back." He was extremely unstable emotionally and presented a peculiar admixture of depression and anxiety. Except for his definite and persistent hypertension, all of his symptoms might well have been explained on a functional basis.

In the absence of other obvious causes of hypertension in a patient of this age group, and in spite of the fact that he had never manifested typical paroxysmal fluctuations in blood pressure with normal readings between attacks, a chromaffin cell tumor was suspected because of these symptoms of marked sympathicotonia and hypertension. On this basis adrenal exploration was thought to be justified and operation was planned. At the end of the third hospital week, although there had been no change in the appearance of his extremities, he began to complain of severe itching and burning of his hands and feet. It then became obvious that a diagnosis of acrodynia would satisfactorily explain the persistent tachycardia and hypertension, cold nose and extremities, reddened itching hands and feet, sweating, bizarre positions, and loss of weight. Treatment was supportive and consisted of a high caloric diet with vitamin supplements and sedation as needed. The symptoms gradually became less marked, his appetite improved, and the patient regained the weight he had lost during the first part of the hospital stay. He was discharged moderately improved at the end of nine weeks.

On return to clinic one month after discharge, he appeared further improved, both physically and emotionally. Hypertension of 180/145 still persisted and he continued to have profuse sweating and severe itching of his hands and feet. The extremities at this time presented the typical appearance of acrodynia, the skin of the hands and feet being thickened and markedly reddened with flaky desquamation over the dorsa and around the nail beds. His condition continued to improve and four months later recovery was complete, blood pressure was not elevated, and his appearance and behavior were those of a normal boy.

DISCUSSION

A case of acrodynia in a 13-year-old boy has been presented. Diagnosis was based on tachycardia, hypertension, pains of a migratory nature, and sensation of burning and itching.

The patient's behavior and unsystematized complaints, together with his agitated mental state and despondency, suggested a functional disorder. Persistent hypertension, however, made a diagnosis of psychoneurosis untenable.

For a time all his symptoms and findings seemed consistent with sympathetic imbalance such as an epinephrine-producing chromaffin cell tumor may cause. The "smothering spells" which were a prominent feature of the boy's illness simulated the paroxysmal sympathicotonia of chromaffin cell tumors, with sensations of precordial constriction, suffocation, flushing of the skin, anxiety, diffuse pains, and profuse perspiration. Although a transitory elevation of blood pressure above resting levels was noted during only one of his attacks, paroxysmal

hypertension is not a sine qua non in the diagnosis of pheochromocytoma. Persistently elevated blood pressure was observed in two patients reported by McCullagh and Engel.[13] In our patient the right kidney was easily palpable and at times massage of this kidney seemed to precipitate the described attacks. Pheochromocytomas are more common in the right adrenal and, in five of the eighteen patients with proved cases reviewed by Howard and Barker,[14] the tumor mass was not demonstrable by palpation or pyelogram. Loss of weight, headache, and emotional disturbances also occur fairly constantly with these tumors. Belt and Powell[15] reported a fatal case of pheochromocytoma in a middle-aged woman, diagnosed at autopsy, whose clinical story had been misinterpreted as being either neurotic or climacteric. Because of these similarities in the clinical picture, a tentative diagnosis of pheochromocytoma was made in our patient, and adrenal exploration was planned. It was not until three weeks after admission to the hospital and three months after the onset of his illness that he developed intense burning and itching of the hands and feet, suggesting acrodynia. Typical skin lesions with marked redness, succulence, and desquamation did not appear until the patient had been under observation for a period of thirteen weeks. Diagnosis was further confirmed by the complete recovery which ensued ten months after the onset of his disease.

Acrodynia in older children does not differ from the disease as described in adults. The main difference in the infantile and adult types seems to lie in the more vociferous expression of complaints and the wider reaction pattern of the older individual. When the characteristic burning, itching, and redness of the extremities appear late in the disease, only the tachycardia and hypertension serve to distinguish acrodynia from a functional disorder, and the clinical picture may simulate that of a chromaffin cell tumor.

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CONGENITAL LEUCEMIA

Report of Two Cases

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THE relative rarity of congenital leucemia occasions the reporting of two cases of myelogenous leucemia, apparently congenital, seen at The Children's Memorial Hospital in the past twenty-five years. Since 1918, 38 cases of leucemia have come to autopsy, 24 lymphogenous and 14 myelogenous. Of this number, eight patients, two with lymphogenous and six with myelogenous, were under 1 year of age (Table I).

Table I

Patients With Leucemia Under 1 Year of Age

YEAR	SEX	AGE AT ONSET	AGE AT DEATH	TYPE
1931	F	3 mo.	5 mo.	Lymphogenous
1934	M	5 days	3½ mo.	Myelogenous
1934	F	10½ mo.	11 mo.	Myelogenous
1938	F	6 mo.	7 mo.	Myelogenous
1938	M	5½ mo.	6 mo.	Lymphogenous
1942	F	3 mo.	6 mo.	Myelogenous
1943	F	At birth	3½ mo.	Myelogenous
1943	F	4 mo.	6 mo.	Myelogenous

The following two cases from the above table are reported in detail.

CASE REPORTS

Case 1.*—R. B., a white, male infant, born March 20, 1934, was admitted to the hospital on June 25, 1934, and died July 7, 1934. He was the only child of Italian parents; the family history was negative; and he had a full term, normal delivery, weighing 4 pounds, 16 ounces at birth. At the age of 5 days and again one week later he bled from the bowels. He was then given intramuscular blood but never did well, had a poor appetite, and failed to gain weight.

On admission, physical examination showed a thin, undernourished, 3-month-old male infant with poor tissue turgor. Petechiae and edema of scalp, abdomen, and lower extremities were present. The liver was moderately enlarged and the spleen extended down into the pelvis. A soft systolic murmur was heard over the precordium. Blood count showed 55 per cent hemoglobin, 2,250,000 red blood cells, and 112,000 white blood cells per cubic millimeter with many immature forms, myelocytes, myeloblasts, reticulated red cells, and normoblasts.

The child received one x-ray treatment, 184 roentgen units, over the spleen, and the white blood count dropped to 84,000 and then to 58,000 per cubic millimeter a few days before death.

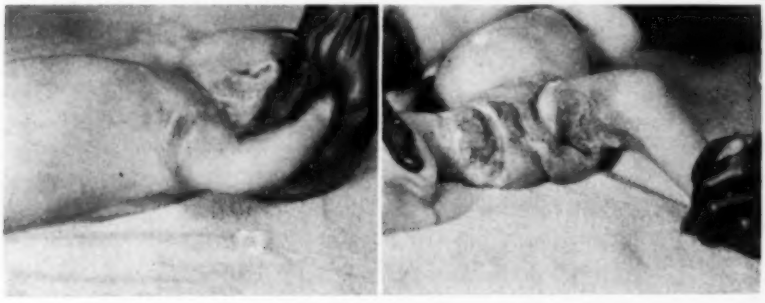
Pathologic examination after death revealed slight enlargement of the liver and enormous enlargement of the spleen, with leucemic infiltrations in the liver, lymph

From The Children's Memorial Hospital, Chicago, Ill.
*Included through the courtesy of Dr. Traisman.

nodes, kidneys, and spleen. There were hemorrhages in the lungs, skin, and the mucosa of the intestines. Slight cardiac enlargement was present with patent foramen ovale and interventricular septum.

Final diagnosis was myelogenous leucemia and congenital heart disease.

CASE 2.—M. McG., a white female infant, born Nov. 9, 1942, was admitted to the hospital on Dec. 22, 1942, and died on Feb. 17, 1943. She was the only child of Irish parents. The family history was negative. The child was born after a normal gestation and normal spontaneous vertex delivery at full term. The birth weight was 7 pounds, 6 ounces. At birth she had a heavy, crusty coating of vernix caseosa (?) which was impossible to clean off the neck, axillae, and groin. These places became excoriated, infected, and large yellow plaques of crustlike scab formed. Subcutaneous hemorrhages were present at birth as well as bleeding from the bowels. The infant was given vitamin K and twelve intramuscular injections of blood. She took feedings well and gained weight. Abscesses and ecchymoses formed at several of the points of intramuscular injection. She continued to have bloody stools.



A. *B.*

Fig. 1.—*A*, Lesions of axilla and neck; *B*, lesions of the labial and buttocks region.

On admission, physical examination showed a well-developed, 1½-month-old infant with good tissue turgor, fairly good color, and numerous dermatologic lesions (Fig. 1). There was a systolic murmur heard over the entire precordium and not transmitted. The liver was felt at the costal margin and the spleen 2 cm. below the costal margin. Cervical lymph glands were palpable. There were a few petechiae on the hard palate. The scalp was dry and scaly. Many petechiae were scattered over the entire body. There was a large hematoma on the left chest and a 2 cm. ulcer over the mid-dorsal spine surrounded by an ecchymotic, red, and indurated area. There were a few purpuric spots on the extremities. Over the axilla, groin, and around the neck and ears, the skin was excoriated and covered with dry, thick, yellow, crustlike plaques of tissue or exudate. Removal of these left a persistently bleeding surface. Blood count showed 5.9 Gm. of hemoglobin, 2,270,000 red blood cells, 72,500 platelets, and 23,000 white blood cells per cubic millimeter with 51 per cent polymorphonuclear leucocytes, 32 per cent lymphocytes, 5 per cent monocytes, 1 per cent eosinophiles, 2 per cent basophiles, 6 per cent metamyelocytes, 2 per cent myelocytes, and 1 per cent premyelocytes. There were many macroblasts and normoblasts present. Bleeding time was over thirty minutes, and coagulation time was two minutes, fifty seconds.

The patient received blood transfusions every few days, a total of 890 c.c. of blood being given during her stay in the hospital. The skin lesions, treated with 2 per cent gentian violet solution while the infant was kept in a heated tent, gradually improved, but the eschar, when removed, left a persistently bleeding surface, and

the neck never entirely cleared up. The spleen continued to enlarge and the purpuric spots, to increase in number. Inguinal adenopathy developed during the last two weeks of life, and the child's color became somewhat greenish in tinge. Ten days before death she developed a cerebral hemorrhage with bulging fontanel, ptosis of left eyelid, and opisthotonos. The blood picture remained about the same as upon admission except for a drop in platelet count to around 35,000 per cubic millimeter.

Pathologic examination after death revealed many eosinophilic myelocytes and undifferentiated toxic cells in the bone marrow, lymph nodes, and spleen. The germinal centers were absent from the spleen. The superficial cornified layer of the skin was missing. The basal layer was greatly thickened. There were hemorrhages throughout all the viscera, cerebral hemorrhages and edema, subarachnoid bleeding, subdural hematomas, and myocardial hemorrhage.

Final diagnosis was myelogenous leucemia, cerebral hemorrhage, and hemorrhage throughout all viscera.

DISCUSSION

These two cases are of interest not only because of the congenital features, but the second case in particular because of its unusual skin manifestations. In myelogenous leucemia of any age, skin involvement is rare except for purpura.[25] In lymphogenous leucemia in children, the skin is seldom involved either specifically as leucemic infiltration of the skin or nonspecifically as leucemids of toxic origin.[7, 8, 18] Occasionally the skin is involved some time previous to the appearance of a leucemic blood picture.[13] In such conditions it has been suggested that the prolonged insult to the skin might be the cause of the leucemia.[23] Such a theory is hardly tenable for our case, however, since the subcutaneous hemorrhages present at birth and the blood picture show that the blood dyscrasia was probably concomitant with or preceded the skin involvement.

TABLE II

CASES OF CONGENITAL LEUCEMIA IN LITERATURE OF PAST TWENTY-FIVE YEARS

YEAR	AUTHOR	AGE FIRST SEEN	TYPE
1921	Smith[20]	Newborn	Lymphogenous
1922	Koch[11] (Cited by Abt[1])	Newborn	Myelogenous
1922	Koch[11] (Cited by Abt[1])	Newborn	Myelogenous
1924	Opitz[15] (Cited by Abt[1])	12 wk.	Myelogenous
1925	Stransky[21] (Cited by Abt[1])	3 wk.	Myelogenous
1931	Bungler[3] (Cited by Abt[1])	Stillborn	Myelogenous
1931	White and Burns[22]	3 wk.	Lymphogenous
1932	Chapman and Ewart[5] (Cited by Morrison and co-workers[14])	Newborn	Lymphogenous
1933	Cooke[6]	4 days	Myelogenous
1933	Cooke[6]	10 days	Myelogenous
1933	Cooke[6]	3 mo.	Myelogenous
1933	Giblin[9]	2 wk.	Myelogenous
1934	Kornmann[12] (Cited by Abt[1])	6 wk.	Myelogenous
1937	Saxl[19]	6 wk.	Myelogenous
1938	Rhamy[17]	Newborn	Myelogenous
1939	Morrison, Samwick, and Rubinstein[14]	Newborn	Myelogenous
1939	Kelsey and Anderson[10]	25 days	Myelogenous
1941	Acuña and Vallino[2]	Newborn	(?)
1942	Chandhur[4]	4 wk.	Myelogenous
1942	Poncher[16]	Newborn	Myelogenous

RÉSUMÉ OF THE LITERATURE

In addition to the two cases here described, twenty cases of congenital leucemia have been found in the literature of the past twenty-five years (Table II). Sixteen were myelogenous, three were lymphogenous, and one was questionable in type. Some twelve or more cases have been reported in the older literature,[12] but because of the crudeness of hematologic technique at the time as well as the possibility of confusion with erythroblastosis fetalis, icterus gravis, and the leucemoid reactions of infections, these cases were not considered well substantiated. The cases reported in the last ten years were found in part by combing the Cumulative Index. The earlier cases for the most part were found in previously published reviews of the literature as indicated in Table II.[1, 8, 12]

SUMMARY

1. Two cases of congenital myelogenous leucemia are reported in detail.

2. A review of the literature of the past twenty-five years reveals twenty cases of congenital leucemia reported, of which sixteen were myelogenous, three were lymphogenous, and one was questionable in type.

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426 W. OTTAWA ST.

SUBLINGUAL GRANULOMA IN INFANCY (RIGA-FEDE'S DISEASE)

Report of Two Cases

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RIGA-FEDE'S disease is a condition which has received little attention from American pediatricians. We have been able to find only three reported cases in the American literature (Amberg,[1] Bray,[2] and Bradley[3]).

In 1857 Cardarelli described an ulceration of the frenulum linguae in cachectic infants. Riga, in 1881, described the localized membrane formation and development of a hard tumor. Fede, in 1890, published the first histologic studies, and reported fifteen of his own cases and five cases of other authors. Amberg[1] has reviewed the rather extensive European literature up to 1903. Since then there have been only two cases reported in the American literature. Several cases have been reported in Europe by Moncrieff,[4] Newman,[5] Abetti,[6] Caminiti,[7] Comby;[8] and in Japan, by Kasahara and Nagatani.[9]

The disease has been reported most frequently in southern Italy. It usually appears in young infants shortly after the eruption of the lower central incisors with or without associated whooping cough. The general conclusion by Moncrieff, who has carefully reviewed the suggested etiologies, is that the condition is an inflammatory granuloma of the frenulum linguae arising as a result of mechanical trauma and secondary nonspecific infection. Early efforts to attribute the disease to a specific infection or to link it with cachexia have failed; the disease has been found in otherwise healthy babies. The mechanical origin has been well confirmed in discussions by Abetti,[6] Comby,[8] and Moncrieff.[4]

The condition is initiated by an erosion produced by the sawing of the frenulum linguae on the sharp, cutting edges of the lower central incisors. With repetition of the trauma and secondary infection, granulation tissue forms and produces a tumorlike mass, which is usually disc-shaped and about 1 cm. in diameter. In the center there is usually an ulcerated area covered with a fibrinous pseudomembrane. The tumor sometimes causes difficulty in nursing, but there are no other symptoms. There is no associated lymphadenopathy or adjacent inflammation.

Two children with this condition have been seen in the Children's Wards of Stanford University Hospitals.

From the Department of Pediatrics, Stanford University School of Medicine.

CASE 1.—B. G., an 11-month-old white female baby of American ancestry, was admitted to the Children's Ward of Stanford University Hospitals on Sept. 23, 1940. The child's birth, delivery, and development were not remarkable. There was no history of pertussis. The lower central incisors erupted at 8 months of age. At about the age of 10 months the mother noted a small white spot under the tongue in the midline. This mass grew rapidly, bled frequently, and seemed to interfere with the child's efforts to talk. The tumor was frequently scraped over the two lower incisor teeth.

On entry a white, raised, pupillomatous tumor of the frenulum linguae was noted (Fig. 1). The frenulum was shortened and the tip of the tongue indented. The tumor was round and flat and had a broad base, about 1 cm. in diameter. There were four upper and three lower incisor teeth. The rest of the physical examination was not remarkable. The blood count and urine examination were normal. The tuberculin test and Wassermann reactions were negative.

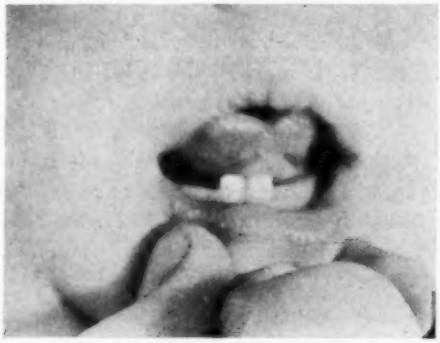

FIG. 1.—B. G., Sept. 24, 1940; age, 11 months. The granuloma is seen under the tongue above the lower incisors. Note the appearance of tongue-tie.

The tumor was excised under ether anesthesia. Recovery was uneventful. The child began to talk soon afterward.

The pathologic report on the excised tumor was as follows: The specimen consisted of a formalin-fixed irregular lobulated nodule ½ cm. in greatest diameter. One aspect was covered by pale, thick, and wrinkled membrane. Other surfaces were ragged. On section this membrane was sharply demarcated from underlying fleshy tissue. Section showed interlacing bands of striated muscle and enveloping fibrinous tissue in which were scattered small groups of glands, the whole covered on one surface by a wide layer of stratified squamous epithelium. This epithelium was interrupted at one point, the surface being formed by necrotic material. Beneath this were very numerous neutrophilic and eosinophilic leucocytes in a vascular fibrous stroma which extended irregularly into more dense underlying stroma.

CASE 2.—J. K., a 9-month-old white American female baby, was referred to the Pediatric Service of Stanford University Hospitals on April 11, 1943, because of a suspected malignant tumor of the sublingual region. The tumor was first noticed about one month prior to entry. Since then it had doubled in size and become light in color, and it had been found to bleed from the slightest trauma. She had been entirely bottle-fed. At the age of 2 months she had pertussis. When the child was 4 months old the two lower central incisors erupted.

On entry the physical examination was negative except for changes in the gums and costachondral junctions compatible with mild scurvy and for the sublingual

tumor (Fig. 2). Below the tongue and moving with it was a whitish mass, 1.2 cm. in diameter, attached to and almost covering the frenulum. It was firm, with a rubbery consistency. There was no evidence of inflammation or regional lymphadenopathy. In this case no tongue-tie was evident. The blood Wassermann reaction and the tuberculin test were negative. Blood counts were entirely normal, without any eosinophilia.

Fig. 2.—J. K., April 15, 1943; age, 9 months. The relation of the granuloma to the lower incisors is well shown.

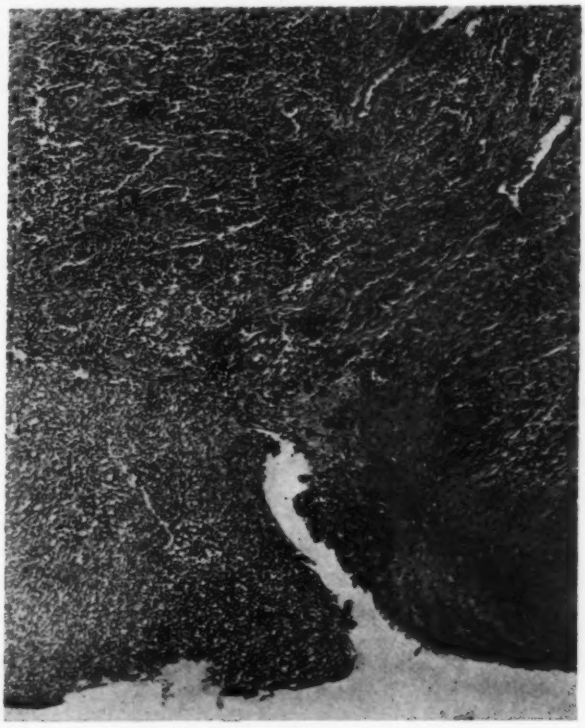

Fig. 3.—Microphotograph of the tumor from patient in Case 2 (low power).

The clinical diagnosis was Riga-Fede's disease. The tumor was readily removed surgically under local anesthesia. The child did very well postoperatively, showing a good appetite and weight gain. On dismissal she seemed to be entirely well.

The pathologic report was as follows: The biopsy specimen consisted of a small formalin-fixed piece of white tissue measuring 4 by 3 by 2 mm. Microscopic sections showed thickened stratified squamous epithelium of the tongue which was suddenly interrupted by an undermining granulating ulcer extending as deep as the biopsy was taken. The ulcer surface was composed of a thick layer of fibrin in which large numbers of polymorphonuclear leucocytes were enmeshed; deeper was a loose fibrous connective tissue stroma containing many small distended vascular spaces and a heavy infiltration of polymorphonuclear leucocytes and plasma cells. Interlacing fibromuscular bundles with fewer blood vessels and a lighter inflammatory infiltration were found at the ulcer base. No tubercles were seen; there was no evidence of malignancy. The diagnosis was ulcer, tongue, subacute, and granuloma, tongue, nonspecific. The microscopic appearance of the tumor is shown in Fig. 3.

DISCUSSION

The patients in the two cases described were treated by excision of the tumors. Both children are well at the present time, and there has been no recurrence of the tumor. The literature suggests many different treatments: removal of the lower central incisors; filing of the rough edges of these teeth; excision of the tumor; treatment of the tumor with caustic chemicals and electrocoagulation. Moncrieff[4] and others report the spontaneous disappearance of the tumor without any treatment or merely by stopping suckling.

SUMMARY

1. Two cases of Riga-Fede's disease are reported.

2. The disease is a granuloma of the frenulum linguae following abrasion by the lower central incisors and secondary infection.

3. Excision of the mass in our patients resulted in prompt recovery.

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FRIED FOOD FOR CHILDREN?

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MOST doctors, if asked whether fried foods are harmful for children and should therefore be forbidden, would unhesitatingly reply "yes." Further, they would feel confident that they were on sound scientific ground in making this assertion. Yet most doctors frequently have fried foods at their own family tables; they permit their patients to eat them; they even include scrambled eggs, lamb chops, and bacon on their diet lists. Even though they may specify broiling, they know that in most homes it is the frying pan and not the broiling flame that will be employed for cooking them.

It has been my custom to forbid fried foods to children, ever since I began to practice. But I believe that any conviction is open to question and should be discarded if disproved. Especially with our wartime shortages is it desirable to be sure of the soundness of our dietary beliefs.

For this reason several months ago I began to look into the basis of this belief that fried foods are harmful for children. Three sources were open to me:

1. Published records of original research.
2. Current books and bulletins, with a critical evaluation of the soundness of the references on which their statements were based.
3. The opinion of living experts in the fields of nutrition and pediatrics.

PUBLISHED ORIGINAL RESEARCH

Strange as it may seem, and considerably to my surprise, I have been able to find only one published piece of experimental research on the subject of fried foods and their effects upon digestion (Boggess and Ivy[1]). The following are excerpts from their work.

"It is generally accepted that fried foods are more indigestible than others. . . . We have devised experiments to prove whether they are or not. . . . Potatoes were chosen because of their universal use, low fat content, simple composition, and ease of uniform preparation."

They summarize their laboratory experiments thus:

"The starch of the pan fried is more easily digested than that of the French fried; and the French fried, *more easily* than that of the boiled potato."

Boggess and Ivy made feeding experiments on two dogs and five human beings. Fluoroscopic observations were made at fifteen- and thirty-minute intervals, beginning two hours after each meal. By this method

the emptying time of the stomach could be accurately determined. They summarize their in vivo work as follows:

Fat actually facilitated the rate of digestion. The gastric motor mechanism of some individuals is more susceptible to the inhibitory action of fats than that of others. In susceptible individuals a gastric disturbance is more likely to be due to disturbed motility than to any decrease in digestibility due to fat. *In the average normal individual,* fried potatoes are no more likely to cause digestive disturbances than are boiled potatoes.

The editor of the *Journal of the American Medical Association* called attention to this article by Boggess and Ivy and the research it described in an editorial, "Food Prejudices and Facts,"[2] in which the banana was cited as one of the examples of changed prejudices and facts.

CURRENT BOOKS AND PERIODICALS

Authoritative textbooks on nutrition, federal and state health bulletins, pamphlets on child care, and so forth abound with diatribes against fried foods, especially for children. Much to my surprise, however, I looked in vain for any scientific verification of what were very evidently simply parroted repetitions of adverse opinions.

For example, a much used government pamphlet on child care contains the following quotations:

". . . nor should any vegetables be fried, even potatoes." (Disproof of this has been cited by Boggess and Ivy.)

"Eggs cooked in fat are not suitable for children." (Common practice of physicians who order scrambled eggs is in direct conflict with this.)

"Fried meats or fried fish have no place in the child's diet. The only gravy used should be meat juice without fat."

"Forbidden foods . . . foods that are . . . cooked in fats should not be used."

Textbooks on dietetics were equally sweeping in their condemnation of fried foods. They were equally without the citation of scientific basis for their statements. For example:

"The disadvantages of fried foods deserve special mention. When *properly* fried, they can be eaten in *moderate* amounts by healthy adults without digestive distress. But they are *always rather difficult to digest* and hence should not be used *too frequently, too many* at one time, or when overtired or unwell. *They should be left out of the diet of children.* In the process of frying, fat is heated to a high temperature and some of it is apt to be broken down into decomposition products which are irritating to the alimentary tract." [Italics mine.] (This last statement will be found to be completely disproved in the opinion of one of our best known nutritionists to be quoted shortly.)

"Use fried foods very moderately, and only when properly cooked."

"In frying, decomposition products are formed, which are irritating to the digestive tract." (The answer to this claim has been mentioned previously.)

"Certain foods are ruined digestively by frying." (It is not specified what foods these are.)

"In the main, frying should be confined to starchy foods, as the protein-rich foods are almost sure to be rendered comparatively indigestible by frying." (How about the protein in our much-favored scrambled eggs?)

The fairest statements regarding frying were those which differentiated between proper and improper frying in a book on dietetics just off the press:

"The stigma attached to fried foods is due largely to carelessness and improper methods of frying. . . When properly done, fried foods eaten in judicious amounts should cause no difficulty to a normal digestion. . . But never should one with a delicate digestion indulge in fried food." (Even here the implication is plainly against frying.)

In all of this, two points are quite clear:

1. The complete absence of scientific basis for the statements made leaves the case against fried foods an authoritarian rather than a scientific one.

2. Condemning *all* fried foods because improper frying may cause harmful effects is neither fair-minded nor scientific. Since nutritionists, home economics schools, women's magazines, cooking schools, and advertising recipes have disseminated so widely a knowledge of what constitutes good cooking, it is reasonable to take it for granted that correct frying is now a matter of common knowledge and that the greasy, soggy piecrust and fat-soaked fried potatoes and doughnuts of the old-time boardinghouse are "out" for good in most American homes of today.

PERSONAL OPINIONS OF LIVING EXPERTS

Inasmuch as so many of our highest authorities have not expressed themselves in print on this subject, it occurred to me that perhaps the best way to continue my research would be to write to persons of acknowledged eminence in this field in the scientific world and ask them frankly their beliefs regarding fried foods together with their reasons for or against their use.

Accordingly, after consultation with Dr. W. W. Bauer, Director of the Bureau of Health Education of the American Medical Association, and Franklin C. Bing, Secretary of its Council on Foods, I made a list of authorities whose opinions seemed to me to be of generally accepted value. This list has grown as a result of much correspondence until now it has reached proportions that may be summed up, or itemized, as follows:

Eleven nutritionists, biochemists, and physiologists, all of whom are heads of departments in approved institutions of learning

Seven pediatricians of nationwide reputation, with private practices as well as teaching positions, welfare appointments, and hospital appointments

Two pediatricians holding key positions in the Children's Bureau

Two gastroenterologists in private practice

One nutrition director of the American Red Cross

Two medical editors

Two research bureau heads

Many of these authorities are personal friends of mine. Others were consulted by these friends, on their own initiative, in an effort to help me get the information I sought.

As this correspondence was so entirely private and personal, it does not seem quite fair to publish individual opinions and quote them, but I do feel free to present some quotations without giving names.

I think it will surprise other physicians as much as it did me to learn that not one of these authorities had a single objection to the frying of foods for children's use such as I had always entertained in common with most of my medical colleagues and had found in published works.

I choose first the opinions of some of the nutritionists whom I consulted.

The head of the department of physiology of a large midwestern university writes as follows:

"So far as I know (and Dr. _____ of our home economics department agrees with me) the theoretical phobia against fried foods, so far as it has any basis, is purely a matter of the amount of fat added to the food. . . The frying has no deleterious action on the proteins, starches, or vitamins that are not induced by cooking or steaming. So far as digestibility is concerned, it is of no significant dietary importance unless the process completely coats or impregnates the food."

A nutritionist from the department of physiology of the school of medicine and dentistry of a large eastern university writes as follows:

"Fried food, if properly fried, should give no more trouble than would food mixed with the fat which the fried food contains. It is my opinion that the warnings against fried foods are largely a hangover from the time when frying meant soaking the food in hot fat."

One of the pioneers in the modern science of nutrition, who has done much to popularize the subject and who is head of the department of biochemistry of the school of hygiene and public health of a famous university, writes the following:

"The basis for the oft-repeated assertion that fried foods are injurious was the undoubted fact that *in a qualitative sense* some fat became heated and incipiently decomposed; likewise, a little of the surface protein was likely to be scorched. Perhaps it was also believed that often

fried foods were not cooked to the point of hydrolyzing collagen, as is the case in roasting or stewing meat. While *qualitatively* these views are well founded, *quantitatively* the changes in the nutrients mentioned are *too small* to be of significance.

"Numerous assays of food made to determine the effects of different modes of cooking on the loss of nutritive value all show very clearly that among the various ways of cooking meat, frying results in the *least* destruction of essential nutrients. In baking or roasting meats, as much as 50 per cent of the thiamine may be destroyed. Emphasis is now being placed on cooking all foods—animal and vegetable—as quickly as possible."

Figures taken from the United States Department of Agriculture* bear this out (Table I).

TABLE I

	RAW	BAKED	BROILED	ROASTED	FRIED
	Thiamine (Vitamin B_1) Content (μg)				
Round beef	290	–	148	132	290
Lean pork	1830	915	–	915	1190
	Riboflavin Content (μg)				
Round beef	290	–	–	165	198
Lean pork (1)	200	91.5	–	–	183
Lean pork (2)	270	–	–	107	122

The professor of biochemistry of the school of medicine of one of the large western universities writes:

"I know of no experimental work on either human beings or animals where it has been shown that the digestibility of the fats of fried foods is any less than that of the fat when fed alone."

To the pediatricians and general practitioners for whom this paper is written, the opinions of practicing pediatric authorities will probably be of more interest than those of the more theoretical research scientists from whose letters I have been quoting. Here are some of them. The first is from one of the oldest and most respected pediatricians of the country, editor of a system of pediatrics that is perhaps the standard authority in this branch of medicine.

"We have had many prohibitions that are not well founded in reason nor in experience. I think, for example, that the idea that fried food is objectionable because of the amount of fat is pretty much bunk; and the fact that perhaps a small part of the food is fried into a condition in which it is not as digestible as if it had not been fried is pretty much in the same category. I believe that a child after the first year, certainly after the second, can eat practically an adult diet, and that it does not make any difference whether the food is boiled, parboiled or fried."

*Circular 638, May, 1942, pages 28 and 158.

From a consultant in a large midwestern city who is also one of the founders and high officials of the American Academy of Pediatrics:

"As a matter of fact, I have long wondered about the use of fried foods for children. It is certainly a matter of folklore that fried foods have been banned. Dr. --------, with whom I talked this morning, said that he had never found any reason for banning fried foods, nor have I. I think it is about as irrational as banning ham and allowing bacon. . . . I am in the same quandary regarding this matter as you and I imagine it is just something that has been handed down from generation to generation."

This following comes from a children's specialist in the same city who is perhaps our outstanding authority on foods and appetite in children:

"I am glad you raised the question of the origin of the fried foods taboo because it is one that has not received the attention it deserves, the unsupported dicta of 'dietary authorities' being generally accepted and followed.

"It is many years since I have forbidden the giving of fried foods to children after they have been weaned; and . . . fried potatoes, fried liver, and other fried foods are and have been used in the regular ward diets for some time. . . . While I, like you, am inclined to think that soaking foods in grease makes them more difficultly manageable by the gastric juices and hence less easily digestible, I do not know that even this is definitely the fact.

"I am sorry that I cannot produce scientific research with which to confound the 'dietary experts' who will not otherwise be convinced, although they are successfully flouted by the everyday practice of good homes and institutions."

The following comes from the dean of one of the outstanding medical schools of the South, who is also a professor of pediatrics:

"I included 'fried foods should be avoided' in my book on pediatrics out of my love and respect for Dr. -------- who is very emphatic on the subject. However, I feel . . . that there is no evidence, experimental or clinical, that fried foods are any worse than any others. I wonder where the tradition started?"

The gentleman just referred to in the above quotation, professor of pediatrics in another college in the Southeast, dashed my hopes of at last finding a prominent pediatrician who would give me scientific basis for opposing the use of fried foods for children by writing me this:

"We medical men are conventionalists and bound by tradition, without thinking or 'trying out.'. . . So all I can say is that fried foods are probably not injurious to infants. Dr. --------, head of our department of medicine, who is leaving us to become professor of physiology at -------- agrees with me almost to the letter."

Still another professor of pediatrics, this time a consultant in New York City, as well as a teacher and a practitioner of pediatrics, contributes this:

"I know of no scientific proof that children should not have fried foods."

A director of research in the Children's Bureau says:

"Fried foods increase the consumption of fats, meats, and carbohydrates at the expense of vegetables and fruits. My personal opinion is that fried foods are not the terrible things we once thought, but that they gain(ed) that reputation because of the fact that they were used to excess."

SUMMARY

A study was made of (1) the literature of scientific research, (2) current published opinion in books and texts and health bulletins and pamphlets, (3) popular beliefs of laity and profession, and (4) the opinions of leading nutritionists and pediatricians expressed in personal correspondence with me regarding the harmfulness or harmlessness of fried foods for children. It led to certain definite conclusions:

1. There is a widely held belief, cherished by physicians and laity alike, to the effect that fried foods are harmful in general and that they are particularly harmful for children.

2. Current textbooks on nutrition and dietetics, pamphlets and health bulletins on child care, and so forth seem, at first glance, to give scientific support and authority for this conviction.

3. An analysis of this material, however, clearly demonstrates that it is not documented with scientific proof or with any proof at all for that matter. Rather, it is merely a repetition and reiteration in many different forms of this unproved old unscientific prejudice.

4. It is interesting to note that many of the statements made against frying indicate that it is *improper* frying technique that has given rise to this wholesale, but unjust condemnation of *all* fried foods.

5. In opposition to these unfounded prejudices, it is the overwhelmingly held opinion of nutritionists, biochemists, physiologists, and pediatricians alike that *there is nothing harmful in properly fried foods for children.*

6. This is borne out by the solitary piece of experimental work discovered in the literature.

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A PSYCHIATRIC CONSULTATION SERVICE IN A PEDIATRIC OUTPATIENT DEPARTMENT

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ONE of the more recent developments in pediatrics is the employment of child psychiatrists as consultants in the various pediatric services. The following review of one consultant's experience in such a capacity is presented with the thought that it may be of interest and help to those pediatricians and child psychiatrists on hospital staffs where such an undertaking already is in operation or to those who are contemplating the institution of such a service.

The clinical experience forming the background for the present discussion includes work as psychiatric consultant in a pediatric outpatient department, a brief period spent in a well-baby clinic to determine the possible indications for mental hygiene during infancy, an experiment in the application of psychiatry in the management of a prophylaxis clinic, teaching of mental hygiene in the public health department of a medical college, and, finally, informal conferences with pediatricians and nurses in one of the teaching health centers of a city health department. The work in the pediatric outpatient department constituted the major part of the experience, six years having been spent there daily as psychiatric consultant on the cases of children whom the pediatricians felt in need of this type of service. At the beginning of that period the project was already well organized and had been in operation for five years.

EXPERIENCES IN A PEDIATRICS OUTPATIENT DEPARTMENT

1. *Procedures.*—The procedure through which cases came to the attention of the psychiatric consultant was as follows: When a pediatrician in the outpatient department felt that a child would profit by a psychiatric survey, the patient was referred to the clerical assistant for a psychiatric appointment, the same routine being followed as in the case of children requiring any other special service, such as that of the endocrinologist, roentgenologist, or ophthalmologist. At the start the consultant saw two patients for psychiatric survey each morning. This amounted to four interviews, as it seemed psychologically sound for the consultant herself to take the psychiatric history from the accompanying parent as well as to examine the child.

The psychiatrist's goal in serving the clinic was to provide as much therapeutic service as possible in addition to making the initial diagnostic

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survey. It soon became apparent that the majority of children being referred presented problems of such complexity that psychiatric treatment over a long period of time was indicated. Only a limited amount of such service could be provided by the consultant, as new patients were continually being referred for examination. This being the case, the more seriously maladjusted children were referred to some regular phychiatric service with adequate facilities for therapy, particularly if the situation appeared to be such that the child and family could make use of treatment. Turning to the children's division of the psychiatric outpatient department in our own hospital was naturally the first move. Here, however, there were so many children already on the waiting list for treatment that very few new patients could be accepted. For this reason only the children with the most urgent and the most favorable cases with respect to therapeutic outlook were referred. An effort was made to route the remaining children with urgent cases to other psychiatric clinics in the city, but there, too, one encountered inadequate therapeutic resources, so that in a short time the consultant was in an unusually pressing situation owing to the fact that cases were being unearthed more rapidly than they could be handled in anything approximating an adequate manner as far as therapy was concerned.

In addition to this relatively large group of children in need of intensive, long-time treatment, there were children with less acute cases but still in need of therapy. In these it seemed suitable to compromise; the consultant attempted to provide what therapeutic service she could in the pediatric outpatient department itself. In such cases, at the end of the first appointment, a tentative diagnostic formulation was made, therapeutic goals were recorded, and the accompanying parent was given as much advice in keeping with the above goals as it was felt could be assimilated; the child was then offered a return appointment in about a month, sometimes two months, for a follow-up interview. In some of these patients little of therapeutic value resulted. In others, where no doubt the consultant had more soundly evaluated the mother's ability to make use of help and her unconscious as well as conscious desire for it, very gratifying therapeutic progress was made. In fact, it now seems that in this group of cases, though the number is relatively small in proportion to the total number of referred patients, where the parents were reasonably well adjusted and could therefore make use of suggestions and advice, lies the more hopeful area in which therapeutic help by the psychiatric consultant in a busy children's clinic can well be applied. This is in contrast to those cases where the parents had neurotic disturbances themselves which were involved in the genesis of the children's pathology. In still a third group were those patients whose problems were relatively more simple or were in an incipient stage, yet very definitely warranting psychiatric assistance. In these cases a diagnostic formulation and a statement of the underlying mechanisms involved were made, and the patient was referred immediately back to the pediatrician who,

it was hoped, with this additional light and some tentative suggestions with respect to the management of the child, would incorporate these in the pediatric handling of his patient. In many instances the results here, too, were gratifying. In other cases, where the pediatrician was less experienced in dealing with the intangibles involved in problems of emotional adjustment, the outcome was less satisfactory.

As is often the case where sensitivity to emotional aspects of clinical pathology is stimulated, the patients began to come in so rapidly that consultations were scheduled as far as two months in advance. As a result, there began to arise in the pediatric clinic expressions of discontent at having to wait so long for psychiatric assistance. In an endeavor to meet this situation, the procedure was modified: Each day the pediatric charts of all children referred for consultation were reviewed by the consultant, the less suitable patients being excluded and appointments being approved for only those who seemed more likely to benefit by consultation. At the same time the pediatricians were individually apprised of the necessity for limitation of the cases to be studied. Also, they were again reminded that the goal of the project was not so much to provide service for all children needing psychiatric care as to demonstrate in a limited number of children the ways in which the management of pediatric problems could be promoted if one kept in mind the needs of the whole child and did not tend to overlook the emotional aspects of his symptomatology. This, of course, caused some dissatisfaction, particularly on the part of those pediatricians who, in their dilemma at being encumbered with so many problem children and problem families, had a tendency to refer those children with a long history of pathologic social adaptation on the part of the family which left him baffled and frustrated because it impeded his efforts at getting the therapeutic results he had hoped for his patient. In general, however, institution of the above preliminary selection of patients for consultation proved to be a sound procedure and one which in time was a factor in helping some of the physicians to select more appropriate children for psychiatric consultation.

In recording the psychiatric findings in the pediatric charts, the consultant followed the practice of using descriptive terms rather than technical language; in fact, at the start a continued effort was made to school herself in the use of such terminology until it became automatic. The purpose, of course, was to facilitate the pediatricians' getting the content of the findings rather than to provide them with technical labels, for all too often, even in psychiatric services, the latter become empty terms which impede rather than promote understanding. The appreciative response of the pediatricians proved that this effort at sacrificing convenient technical terminology for descriptive language was worth while.

2. *Results.*—It is unsound, of course, to attempt to evaluate on the basis of impression what a consultation service such as that outlined

can achieve. The reliable way in which to measure such achievement would be to make a statistical study of the outcome of the cases after a period of years. Such a study should also include interviews with the referring pediatricians to ascertain their opinions regarding the value of the consultation service to them. To my knowledge such surveys have not been made.

One gets the impression that through the consultation service described, some gains of a sound nature have been made. The outstanding gain seems to be that some of the attending pediatricians have gradually incorporated hitherto unfamiliar psychologic principles into the management of their patients not only in the clinic but in private practice as well. On the other hand, there is danger of wishful thinking on the part of clinical psychiatrists engaged in such projects, as well as those agencies promoting such undertakings; thus achievements may be evaluated in rosier terms than is warranted. Overzealous promotion should be guarded against, for it may leave the pediatrician with resistance to psychiatry and everything it represents. It should be determined carefully whether the well-meant introduction of psychiatry into another specialty from without is as sound as that offered in response to a genuine desire for it coming from the individual pediatricians themselves and from the department in which they are engaged as clinicians. The answer can be given only after all the various factors inherent in a department of pediatrics have been studied carefully. In some localities, the procedure described may be fitting. Elsewhere considerable modification may be necessary.

3. *Suggestions for Establishing a Psychiatric Service in a Pediatric Clinic: Relationship Between the Pediatric and Psychiatric Departments.*—In deciding to introduce psychiatric consultants into a department of pediatrics, one must take into consideration the relationship of this department to that of psychiatry in any given hospital. In order to obtain the highest type of work, the psychiatrist must be under the direction of the department of psychiatry. His work must be judged by his peers. Without close contact with other psychiatrists he will become isolated. He will be unable to develop with the constant growth of psychiatric knowledge and may tend to become entirely practical minded and thereby less searching and critical. In institutions in which the department of pediatrics is isolated from that of psychiatry, the psychiatric consultant should be urged to establish a formal connection with the department of psychiatry in that community. In cases of complete isolation it is especially important for the psychiatric consultant to join psychiatric societies and attend their meetings. Time and, if possible, financial support should be offered liberally for this purpose.

Goals: It is important at the outset to have a clear delineation of goals. For example, much time and experimentation can be saved if it is decided whether the objective is to provide general psychiatric service for all of the children in the pediatric outpatient department who

need it, or whether, on the contrary, the aim is to demonstrate the possibilities which psychiatry offers in the management of typical psychiatric situations arising in a pediatric service. Again the purpose may be to inculcate in members of the pediatric staff additional appreciation of the emotional aspects of pathology encountered in pediatric practice and to provide them with techniques for more adequately dealing with such problems; or finally, one may decide to give the pediatric service a little of all of these types of psychiatric assistance. In the last analysis, if there is the usual limitation of available psychiatric service, it comes down to whether the psychiatric consultant is going to spread his assistance out thin or do a first-rate piece of work in a limited area. After considerable experimentation in attempting to achieve these various goals, it has seemed to the writer that in introducing psychiatric management into a pediatric outpatient department the consultant might well confine his efforts to preschool children. In the first place, this is probably more accurately pediatric psychiatry; in the second, it is more apt to exclude automatically the well-developed, fully crystallized cases of psychopathology and mental retardation which, because of the impact they make on a busy pediatrician, are turned over to the psychiatrist first in a service where psychiatric assistance has previously been unavailable. Confining oneself to the problems of the preschool group will give the consultant plenty to do, not only with respect to quantity, but also with regard to complexity of psychopathology in need of psychiatric management. The markedly ill child in the older groups should be directly referred to some psychiatric clinic or institution which is prepared to provide the intensive, prolonged treatment which such pathology requires.

Selection of Patients: Regardless of the area to which the psychiatrist decides to confine himself and the deliminations agreed upon, the chances are that even within the chosen area sooner or later it will become necessary to make a secondary selection of patients on whom to confine his efforts. Realizing this, he will from the outset spend considerable time with the pediatricians on the staff, helping them to understand what are the more appropriate cases for referral to the psychiatrist and assisting them in becoming familiar with the criteria for such selection.

In considering such criteria, we might well divide them into two classes: (1) those having to do with the child's environment, particularly his family, and (2) those pertaining to the child himself. In connection with the former, it is most important for the physician to distinguish between psychiatry and social service. Unfortunately, even on the part of some psychiatrists, clear thinking on this point is lacking. Actually the difference between psychiatry and social work is as distinct as that between orthopedics and social work, and, to the soundly trained psychiatrist, the symptomatology, underlying mechanisms, and treatment indications are as clear-cut as are the more visible deviations from normal presented by the orthopedic patient. Social service, where

it is indicated as an adjunct in a treatment plan, may be of great value to the psychiatrist, as it often is to the orthopedist, but by the very nature of the exacting medical training which the well-grounded psychiatrist has undergone, social work is never a substitute for his skills.

Where the needs in a given child's situation are predominantly those requiring social adjustment or the services of community resources such as those providing educational, recreational, economic, or protective assistance, the child should be referred to the social worker. If more careful analysis is done in such cases before referral is made, this will reduce waste of psychiatric service. For example, if a child is found to be so flagrantly neglected that on the face of things the first step indicated is court action, or if the family is so poor that the child is underweight because of lack of food, the principle of "first things first" indicates that at this point the aid of social service in meeting the problem is the appropriate measure. If more time and thought were given to the selection of appropriate patients for psychiatric referral, we would find ourselves less frequently in the unfortunate situation where the psychiatrist's time is consumed with referring families to appropriate social agencies, while the social worker is struggling with the "therapy" of a problem mother, for example, which is wholly beyond the scope of her training. Psychiatry, it should be remembered, is a branch of medical science, and it has to do with the recognition and treatment of all kinds and degrees of personality disorders.

Still considering factors in the environment as they bear on criteria for selection of patients for reference to the pediatric-psychiatric consultant, there are the cases where it is clear that it is the parent who is in need of psychiatric examination and treatment. Often such a parent is suffering from one of the various neuroses or from a borderline psychotic condition. In these, the parent himself should be referred directly to an appropriate psychiatric service for adults. Obviously a child in such a situation is already heavily enough burdened and should not be required to go through psychiatric examination for the purpose of getting his parent to a psychiatrist unless all other measures have been exhausted. There is danger in such situations of unwittingly exploiting a child because such a course is the easiest way.

With regard to the second category of criteria, those having to do primarily with pathology in the child himself, one of the first principles to bear in mind is that the referral should be made on the basis of positive psychiatric findings, this in all cases, whether with or without physical complaints. Too often in patients with physical complaints the referring physician proceeds on the old "either, or" premise; that is, on the basis that symptoms are either somatically or functionally determined, and his reason for referring a child for psychiatric consultation is the absence of physical findings in the patient with physical complaints. Much unnecessary shopping around at clinics will be spared the child if the importance of positive psychiatric findings as criteria for re-

ferral is kept clearly in mind. The time will come in well-conducted pediatric services when not only this will be a routine procedure but when the practice, already followed by some pediatricians, of recording the positive findings (historical and/or clinical) regarding the child's emotional adjustment which indicate the need for a psychiatric survey will also be followed routinely.

Even where all the above considerations are borne in mind in selecting appropriate patients for referral, it will still be impossible for the consultant to see every child who warrants a psychiatric examination in clinics where psychiatric service is limited. An important criterion in any further necessary selection of patients is the degree of the mother's interest in having such assistance and the absence of psychologic obstruction within herself to making use of such help for the child. These may seem intangible matters, but conscious and persistent effort at evaluating them makes it much more possible to assay them than is generally supposed. If the psychiatrist's time is unduly occupied with cases in which it is obvious that the mother is so resistive that she cannot use suggestions regarding the psychologic management of her child, little time will be left for assisting the child whose mother is more able to accept such help.

Geographic and economic considerations are also sometimes important. Preference should be given to those patients to whom distance or carfare, for example, are less apt to come up as practical obstacles. Again, care should be taken to preclude patients who are able to afford private psychiatric care, so that the appropriately referred patients who, of necessity, must get their psychiatric help from clinics will not be unnecessarily excluded. Because child psychiatry has been so actively promoted by social agencies, it is the "free" child psychiatry services which are better known; thus it is more natural for parents to turn to such clinics rather than to psychiatrists in private practice. Also, it is easier for those inclined to exploit clinical facilities to do so.

If careful selection of patients is made, much will be gained: little of the psychiatrist's time will have to be spent upon inappropriate referrals; the pediatrician will be relieved of any uncomfortable feeling that he may have been transferring all troublesome cases to psychiatry; and finally, by virtue of the fact that appropriate selection of patients for referral necessitates clearer analysis of the problems involved in a given child, the pediatrician will have his own psychiatric insight enhanced and his medical handling of all patients, regardless of where he encounters them, will be enriched. As an incidental gain, concentration on helping the pediatrician to select suitable patients for referral will accomplish a great deal in enhancing his ability to keep in mind the child as a whole.

Preparation of Parent and Child for Referral to the Psychiatrist: To those who are not actually functioning in a clinic with a psychiatric consultation service and who, for the first time, are considering the fac-

tors determining the various decisions which must be made regarding the mechanics of such a service, it may seem astonishing that procedures in this connection have not already passed through the evolutionary stage and been put in smooth running order. One must remember, however, that the whole specialty of child psychiatry is in the process of evolution and that particularly in pediatric psychiatry we are only beginning to find our way. In this connection it is not at all unusual to learn that, even in a fairly well-established pediatric psychiatry service, one still finds considerable waste of time because of broken appointments with the psychiatrist due to the fact that while the pediatrician was ready for the referral and alert to the need for psychiatric handling of a given problem, the adult who has the management of the child in hand, often the mother or mother substitute, is not ready for such a plan. This is a matter in need of much more attention than it has so far been given. It might be profitable, for example, to make an analysis of broken appointments.

One reason for broken appointments is the parents' fear of psychiatry. Even in the larger cities where there is more sophistication with respect to modern psychiatric practices, the word psychiatrist still carries considerable stigma. For this reason it has been argued that it would be well to have the pediatricians as a matter of routine use some other less disturbing term than psychiatrist in referring to the consultant; for example, child guidance doctor. It is true that the service which psychiatry is rendering these children differs greatly from the type of service provided by the specialist who, twenty-five years ago, was designated as psychiatrist. Change in function has gone in advance of change in terminology. On the other hand, obstacles and prejudices can be overcome if the pediatrician understands fully the meaning of modern psychiatric study and treatment and takes sufficient time to explain his reasons to the parents. The well-informed pediatrician will usually succeed in educating the parents if he recognizes this as his task and is willing to spend sufficient time and effort. This contact with the parents should be considered the first phase of active psychiatric treatment. In case of considerable difficulties in the matter of preparation, the pediatrician should seek advice from the psychiatrist. It is obvious that this way of attacking the parents' misconception is far superior to resorting to subterfuge and to putting the task of educating the parents entirely on the psychiatrist.

Psychiatrists should spend considerable time with the pediatricians to help them see that there is a fundamental difference in referring a child to a roentgenology service, for example, and referring him to a psychiatrist. The latter will be dealing primarily with the emotional problems of the patient and those of his parents through which the psychopathology has developed. Consequently there is bound to be more resistance to accepting the service. The pediatrician who appreciates this will spend time with the parent explaining in simple terms why he feels such a

referral is important, what the mother and child may expect on reaching the psychiatrist's office, and what, in general, are the procedures employed by a psychiatrist in the examination and treatment of a child. It is astonishing how many intelligent and well-informed parents still have little understanding of these issues. The responsibility for this obviously devolves not upon the parents but upon psychiatrists and pediatricians and may partly be due to the fact that the availability of concentrated funds which our economic system has made possible has encouraged the too rapid and too one-sided promotion of child psychiatry.

It is important, too, that the pediatrician not only prepare the parent for the child's referral to the psychiatrist but that he also discuss it with the child. A safe guide to follow with respect to the lower age limit of children who can take in something of such conversation is that by and large children younger than one realizes understand something of what is being said about such matters. Besides the obvious reasons for taking the referral up with the child, there is incidental gain. The writer has often had the experience, after talking such matters over with a child, of finding that the mother comes to appreciate that her child is taking in more of what is said about him in his presence than she realized.

One unfortunate by-product which may result in the course of establishing a psychiatric consultation service in a pediatric clinic is that the pediatricians may come to look upon psychiatry as "just common sense." Such an outcome may be partly due to the psychiatrist's using nontechnical terms and presenting his therapeutic plans in as simple form as possible. Probably a more fundamental cause is the unconscious need of many doctors to oversimplify the dynamics of human behavior, since the physician who becomes more fully aware of the complexities underlying his patient's behavior is going to be more heavily burdened with responsibility for doing something about them.

The tendency to exalt common sense defensively has been excellently discussed by the editors of Child Study.[1] They say:

> Parents, of all people, have a right to ask what science knows about children, and especially about whatever information can be of use to them in their homes. At the same time, and contrary to this wish *to know*, there is apparent a parallel wish, *not to know*. It is interesting with what avidity the press and the public seize upon what they love to call "old-fashioned common sense" as the beginning and end of what is needed to rear children. They love nothing better than to hear that this is all it takes to bring up children, and to stop bothering. Common sense, to be sure, is a very desirable thing to possess, and there are many times when the lack of it is the only thing that is wrong. But this is not always the case. Uncommon sense—expert knowledge—has played the major part in human progress. Common sense is, in fact, ridiculously over-rated and usually by those who possess it least. By itself it would never have discovered that the world was round, or eliminated smallpox, or found that micro-organisms cause disease, or taught us to fly. All these discoveries, before they became acceptable, had to buck the common sense of the day which pooh-poohed them as absurd impossibilities.

It has become a truism to point out that with all the scientific advancements of our age, little has been done to adapt these discoveries to the inner emotional needs of mankind and so to increase expectancy of happiness along with expectancy of life. More and more we are recognizing that the problem of human unhappiness is the biggest problem with which the future has to cope. But it is not generally understood the extent to which this too must become a scientific problem. We are too used to thinking of it as a spiritual problem, or, especially today, as an economic one. In part, of course, it is deeply bound up with both of these, but there remains a large, mysterious residue of people whom religion, philosophy, nor the good things of life have saved from neurotic misery.

We would like, if we knew how, to raise children who are strong in spirit as well as in body. Our deepest hope is that parents will never leave off demanding that science shall regard this matter as its legitimate province and that step by step it will place whatever knowledge it can in the hands of parents everywhere.

OUTGROWTH OF CLINICAL ACTIVITIES

1. *Manual for Pediatricians: Psychological Aspects of Pediatric Practice.*[2]—As an outgrowth of the psychiatric work in the pediatric outpatient department the consultant was asked to collaborate with one of the pediatricians in writing a section in a pediatrics text on the psychiatric management of common problems encountered in the practice of pediatrics. In preparing these articles, emphasis was placed on the dynamic factors in children's symptomatology and behavior problems, also on the use of nontechnical descriptive language in discussing these matters. Apparently publication of this type met a need, for there has been a substantial demand for reprints of the articles.

2. *Prophylaxis Clinic.*[3]—Adapting his endeavors to the particular needs of the pediatric service in which he works, the psychiatric consultant will be prepared for unexpected developments. In the course of the writer's work one such development occurred by virtue of the fact that most of the members of the staff in the prophylaxis clinic, to which children from the general pediatric outpatient department were referred for inoculation, had become concerned about the marked amount of screaming on the part of the children who had to have "the needles." After the pediatrician in charge of this particular clinic and the psychiatrist spent some time in obtaining a perspective on the situation by observing the management of the children as they passed through the clinic, the pediatrician reorganized the techniques used, giving more consideration to the child as a person and to the high incidence of anxiety which was stirred up in the clinic. After trying out these changes in technique, which placed emphasis on reducing the unnecessary anxiety previously aroused, the procedures found to be sound were adopted as a part of the clinic routine. They included such simple modifications as increased gentleness on the part of the admitting physician in making the throat examinations, reduction of the patient's waiting time by staggering appointments, establishment in the child pleasant associations with the

clinic by providing suitable toys, books, and games for his entertainment while waiting for his doctor, special management by the pediatrician for the child suffering from acute neurotic anxiety, reduction of the unnecessary display of such instruments as syringes and needles, and permitting the less excitable mothers to remain in the treatment room during the child's inoculation. Also, in the case of the child old enough to understand, the physician explained the purpose of what was to be done. It was found that children as young as 3 years of age were able to understand something regarding the necessary procedure if it was explained in suitable language. Physical restraint was reduced to a minimum and after the injection was completed, the physician took time for pleasant interchange in order to assure the child of his friendliness. The employment of these newer methods in the prophylaxis clinic was fruitful, for the children, having a better appreciation of why they were subjected to these painful procedures, became less disturbed and more cooperative, and the clinic became peaceful.

3. *Modifications in Technique of Taking the History.*—On beginning work as psychiatric consultant, the writer wondered if the type of history then taken in most child psychiatry clinics was not somewhat static so decided to try different approaches in getting the child's psychiatric history. Having become interested in the dynamic aspects of children's problems, she experimented in the use of a history outline which concerned itself primarily with ascertaining the emotional responses of the child as he passed through such fundamental life experiences as feeding, weaning, toilet training, and first awareness of sexual manifestations. In doing this the emphasis was placed on *how* the child came through these experiences rather than *when*. This experimentation proved worth while, for shortly it transpired that the examiner was able not only to get at the underlying dynamics of the presenting problem much more accurately, but also much more quickly. With this change in emphasis on the part of the psychiatrist in taking histories there was a consequent immediate shift of interest on the part of the more open-minded pediatricians with respect to dealing with general pediatric problems. To be specific, more pediatricians became interested in the emotional aspects of a child's feeding experiences, for example, than in the feeding schedules and the type and amount of nutrition taken.

4. *Investigative Results.*—With the above modification in the technique of taking psychiatric histories, the consultant soon came to realize that these histories were building up a volume of dynamic material of unusual significance. Because of this it was decided to record routinely information on all the areas of dynamic experience in a child's history, regardless of the direction in which the patient's symptoms invited inquiry. This accumulation of material not directly pertinent to the immediate clinical problem was undertaken for the purpose of possible future research. The following studies have resulted from that plan.

THE INCIDENCE AND CHARACTER OF MASTURBATION THREATS IN A GROUP OF PROBLEM CHILDREN[4]

A review of the data on this subject recorded in the children's psychiatric histories was undertaken as an outgrowth of the psychiatric observations made in the pediatric prophylaxis clinic, where it was discovered that the child responding with acute anxiety to the clinic routine was frequently one who had previously been threatened by his mother that if he touched his genitals he would injure himself and have to be taken to the doctor for treatment or surgical care.

A survey regarding the age at which the problem children were first known to have masturbated and the manner in which the masturbation was dealt with by the parents gave interesting facts. Of 320 problem children, 142 were observed to have masturbated; of these, 54 per cent were known to have done so before the age of 5 years. Forty per cent of the 320 were dealt with destructively concerning masturbation. The measure most frequently employed was direct threat and usually the threat was drastic. Physical threats were most often made and in over one-half the children where this was the case, the child was threatened with genital injury. The findings are of interest in that they present factual information corroborative of the Freudian concept of "castration threat." This is important because of its implications with respect to the generation of castration anxiety. The findings differ from Freudian theory in that they reveal the "castrating" agent to be not the father, but the mother. This is provocative and, if given further consideration and study, might lead to a better understanding of the part which the neurotic mother plays in the development of neurosis in her child.

For the prophylaxis of anxiety, a fundamental component of neurotic disorder, it is therefore important that physicians assume the responsibility for reducing through education of the parents the frequency with which such threats are employed. A survey of the literature regarding advice as to the management of masturbation indicates that a most important task is to get across to physicians and parents sounder advice than the punitive measures which writers usually recommend. Fortunately since the above survey was made pediatricians have frankly recognized this need. In the recent edition of one of the outstanding textbooks of pediatrics fundamental changes have been made in recommendations regarding the management of masturbation.

PSYCHOPATHOLOGICAL DISORDERS IN THE MOTHER[5]

During the first years of operation of the consultation service, there was no psychiatric social worker on the consultation staff; therefore it was necessary for the psychiatrist to take the psychiatric histories instead of having them obtained by a social worker, as was the usual practice in child psychiatry services. As a result the writer had the unusual experience of encountering at first hand the psychopathology of the mothers of

problem children. The result was a growing impression that the seriousness of the psychopathology of these mothers was not sufficiently known nor the damage it causes to the personality of the developing child fully appreciated. These observations and the findings in the masturbation survey led to a systematic study of these mothers in the hopes of gaining a better understanding of their psychopathology.

The study revealed that of 488 problem children, 203 of the mothers, or 41 per cent, were suffering from psychopathologic conditions. Of these mothers, the thirty who had been examined or treated in the psychiatric outpatient department for adults suffered primarily from psychoneurotic disorders. Their pathology was complex, and in each case it was an important factor in the problem of the child referred to the psychiatric consultant. Even at the hands of very able and experienced psychiatrists, these mothers proved peculiarly difficult to treat because of their firmly established pattern of projecting their failings onto their children. These findings raised the question of the wisdom of delegating such mothers to social workers, as was then the general practice, and indicated the need for the devotion of more time on the part of psychiatrists themselves to advancing their knowledge regarding the peculiar nature of the psychopathology of these mothers and to evaluating the part it is playing in the development of difficulties in their children. Such tasks, it would seem, constitute one of the present frontiers for psychiatrists who are interested in prophylaxis.

THE CHILD'S RESPONSE TO COERCIVE BOWEL TRAINING

The investigation of the management of bowel training in the problem children examined in the psychiatric consultation service of the pediatrics clinic was the natural outgrowth of obtaining dynamic anamneses. In this study, it was found that the resistance of the mothers to discussing bowel training was considerably greater than to talking about the children's sexual behavior. It was as if the mother realized it was not the child who could be blamed for the undesirable things that occurred in the course of the training but that she sensed culpability in herself. The study revealed that bowel training was being started much earlier than was healthy from the point of view of the child's total development and much earlier than even many of us psychiatrists realized. A review of the literature on bowel training made the surprising discovery that even highly esteemed agencies having the interests of the developing child at heart had been disseminating literature to parents which advised beginning the training unduly early. This is not surprising in view of the fact that only in recent years have pediatricians ceased being primarily concerned with the physical aspects of infancy and given due consideration to the infant's emotional life. Fortunately the more progressive agencies promoting parent education have now begun to modify their advice in keeping with more modern thinking.

The study of the reaction of children to coercive bowel training demonstrated that frequently the child's response was in terms of symptoms through which neurosis often expresses itself. The conclusion seems warranted that adequately meeting such important problems as bowel training is a very fruitful field for pediatric psychiatry.

Recently it has come to the attention of the writer that many pediatricians are discouraged because they are coming to realize that so many problems in their patients call for the help of the psychiatrist. As pediatric psychiatry more adequately contributes what it has to offer, the pediatrician, instead of being discouraged, will be stimulated by the great field of work which will open up for him; namely, opportunities for the sound psychologic management of the incipient problems of the infant and preschool child. Emotional disorders rarely come to the psychiatrist's attention at that early stage, and no doubt they will always fall more appropriately within the province of the pediatrician.

THE ROLE OF THE PSYCHIATRIST IN A WELL-BABY CLINIC[7]

The increasing awareness of need for psychologic management of incipient maladjustment in very young children and the coincident impact of fully crystallized and severe psychopathology in children as young as 6 or 7 years which one sees in a large pediatric clinic led to an investigation of the possibilities of discovering incipient pathologic reactions in infants. Three brief periods were spent in the well-baby clinic of the pediatrics department in an attempt to ascertain what problems, if any, were already appearing in the infants; also, what contribution psychiatry could make to the management of these incipient problems and to the prevention of pathologic adaptation during infancy. The more outstanding findings of this study include the following: an unexpectedly high incidence of unhealthy adaptation on the part of the babies due to unwholesome management of them by poorly adjusted mothers, the surprising discovery that on the advice of well-trained obstetric nurses toilet training had already been started in the case of some of the babies as young as from 4 to 8 weeks, and that suppositories as educative aids were used in nine of the fifty-seven children covered by the study. On the other hand, the incidence of well-adjusted mothers was higher in this special clinic than was the case in the psychiatric consultation service where problem children are routinely seen for examination. Many of the mothers expressed genuine interest in the opportunity for conferring about some of the more subtle questions in regard to their children's development, such as those having to do with emotional adaptation. Thus the survey left one with the impression that in the medical supervision of babies much of interest and value is waiting to be done in the promotion of the healthy adjustment of these children. It is quite possible that one important function of pediatrics may be the improvement and enrichment of techniques for the management of the

psychologic aspects of infancy. It is obvious that much can and should be done on the part of pediatricians and psychiatrists working together toward this goal.

TEACHING MENTAL HYGIENE IN PUBLIC HEALTH

1. *In a Medical College.*—An outgrowth of the consultation service in pediatrics was the invitation to participate in mental hygiene discussions in the fourth year course of the Department of Public Health of Cornell University Medical College. For each mental hygiene session four students were selected, each of whom was to present the case of a child suffering from some psychopathologic disorder. In class discussions of maladjustment in children it is inexpedient to have the patients appear before the students because to children such an experience is too disturbing. As a compromise, emphasis was put on the student's giving as vivid a description of the child whom he had studied as possible. By and large the students entered into these clinical exercises with enthusiasm, to the benefit not only of themselves but of their classmates. No doubt one reason for the latter is that students know their classmates better than we do and are therefore more able to "talk their language."

The selection of problems to be presented in these exercises was determined largely by the type of deviation from normal which happened to come to the students in the course of their work as clinical clerks in the pediatric outpatient service. The first exercise for example was concerned with "Aggression in Childhood," three of the four students having encountered this problem in the pediatric clinic. This not only afforded an opportunity for a theoretical discussion of aggression per se but helped to sharpen the diagnostic acuity of the students through the necessity of determining the underlying cause of the aggression in each case. In one child the aggression was a manifestation of underlying anxiety. In another it was due to constitutional factors in a mentally deficient child whose mental defect had previously been unrecognized. In a third, the aggression was a wholesome response to an unwholesome situation; namely, the pathologic domination of the child on the part of his parents. Other topics which have been presented clinically in subsequent mental hygiene exercises have included the problem of anxiety and its various clinical manifestations: for example, inhibition of intellectual functioning in a child with normal mentality, inhibition in eating, and withdrawal from normal social relationships with other children. A third general topic which came up for clinical presentation was functional gastrointestinal disturbances. In the preparation of his case for presentation, each student was assigned readings to acquaint himself with modern theory in connection with the clinical findings to be discussed.

2. *In a Child Welfare Station of a Public Health Department.*—Because one has to deal with so many variables in teaching pediatric psychiatry, it cannot always be anticipated what direction the spread of the teaching may take. Out of the psychiatric management of problems in

the pediatric outpatient department, the consultant was invited to confer informally with small groups of pediatricians and nurses in a child welfare station of the City Department of Public Health. This was a demonstration health center to which came doctors and nurses from other child welfare stations in the city for study, new contacts, and gaining familiarity with recent theories regarding psychologic problems encountered in their daily clinical work. The consultant proceeded tentatively, adapting the teaching to the interests and needs of the groups as indicated by their questions. The results have been gratifying and have led to the organization of a program of regular seminars of this type. Throughout these discussions it was emphasized that agencies of this type should concern themselves with the minor deviations of the normal preschool child and with incipient psychopathology, not with the more complicated, fully crystallized behavior disorders which should be treated by a psychiatrist. Minor problems will be making themselves known to the child health stations long before they ever come to the attention of the psychiatrist. In the last analysis, therefore, it is the pediatricians, rather than the psychiatrists, who have the opportunity of practicing mental hygiene in its true sense; namely, keeping well children well and doing this in the crucial formative period of the preschool years.

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Errata

In the article by Levine, "The Pathogenesis of Erythroblastosis Fetalis," which appeared on page 656 of the December issue of the JOURNAL, the following corrections should be noted:

p. 661—Table III, heading of the last column should read "Anti-Rh_1" and not "Anti-Rh'."

p. 665—in line 3 the last two words should read "Rh+ blood" instead of "Rh- blood."

p. 667—line 6 of last paragraph should read "Rh+" instead of "Rh-."

p. 669—Table IX, line 4, the percentage of Rh+ among American Indians should read "99.2" instead of "92.2."

In the article by Ingraham and Matson, "Subdural Hematoma in Infancy," which appeared in the January issue of the JOURNAL, line 11, first paragraph, page 1, should begin: Davidoff and Dyke.[2]

American Academy of Pediatrics

Proceedings

TWELFTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

CHICAGO, ILL.—NOV. 5, 1942

Panel Discussion on Pediatric Gynecology

Chairman: Goodrich C. Schauffler, M.D., Assistant Clinical Professor of Obstetrics and Gynecology, University of Oregon, Portland, Ore.

Associates: Edward D. Allen, M.D., Associate Clinical Professor of Obstetrics (Rush), University of Illinois College of Medicine, Chicago, Ill.

Carl G. Ashley, M.D., Clinical Instructor of Pediatrics, University of Oregon Medical School, Portland, Ore.

Elmer L. Sevringhaus, M.D., Professor of Medicine University of Wisconsin, Madison, Wis.

The Immature Female Genital Tract (Practical and Philosophical Considerations)
Goodrich C. Schauffler, M.D., Portland

Injury to the External Genitals

Simple Injury.—Simple injury to the external genitals is surprisingly infrequent when we consider the rough and tumble existence of the younger child; the lack of protection afforded by modern garments; the relative exposure of the vulvar area to trauma contingent upon less recessive genitals, and the lack of pubic hair. Perhaps one reason for the comparative immunity of this region involves an unconscious protective mechanism in the child, contingent upon a peculiar cross connection in the conduction of touch stimuli from the genital area to the little girl's consciousness. It is a rather peculiar and interesting fact that female children, from about the age of 2 years forward, begin to sidetrack even gentle touch stimuli from the vulvar region into paths which register in consciousness as fear or pain. I have made this test so many times that there can be no mistake about it. From the gentle touch of a cotton applicator in the genital area the average child will feel *pain* or experience *fear*. The development of this response may be artificial, but the peculiar response itself is actual. If we choose to regard it as natural may we not suppose that it is a protective mechanism calculated to isolate the immature genitals prior to their readiness to assume their adult biologic function? This matter, of interest in relation to self-protection, is also very important in the approach to diagnosis and treatment. It must enter into the rationale of the conduct of any genital examination in the young girl.

The substance of the clitoris is true erectile tissue—that of the labia, fourchet, hymen, and vaginal wall very nearly so. This implies that the tissue is exceedingly vascular and definitely areolar in type. Injuries bleed profusely but seldom long, and free vascularity appears to account for a remarkable immunity from subsequent infection. Healing proceeds with astonishing rapidity, and the restoration of normal contours is remarkable. Plastic repair, if required, seems to offer a more favorable outlook than elsewhere. Why cannot we assume that the obvious tendency of tissues in this area to with stand injury and to heal rapidly and well is an early manifestation of the natural adult tendency which fortifies this region during and after childbirth in the adult?

Simple trauma to the vulvar area is not uncommon. The child, for example, may injure herself by a fall in crossing a fence or may fall painfully across the bar of a bicycle. Sharp objects may be encountered accidentally. Local reaction to such an injury is characteristic: *Edema* formation is early and copious. It may be the only visible evidence of injury, may be massive, but seldom requires more than the horizontal posture, the application of cold, or occasionally early pressure, for its control. *Hematoma* formation is frequent and may be massive; again, its control is generally not difficult. Undue alarm need not be felt; only rarely will it be wise to evacuate large hematomas under pressure by small incisions. Infection developing in a hematoma may occasionally create a real threat. The treatment is surgical. Injuries up to this point should seldom require surgical consultation otherwise. Pressure and cold at bed rest should be sufficient. *Bleeding* from vulvar injury is often profuse but generally transient and most often self-controlled: again, continuous pressure is of value and should be applied early, and, if ligatures are not at hand, packing of the wound is apt to be effective. Occasionally the ligation of vessels may be necessary but should this be the case, the cavernous nature of the tissue more often requires suture compression of the entire area.

Rape.—This discussion requires at least a brief consideration of the distasteful subject of rape. For the purposes of my own rather meager record of observations in the matter, I would value very highly a count among your members of the number of men who have actually recorded proved rape cases in clinical practice. By this term I imply the use of force to compel the act of intercourse and not the generally accepted connotation which, in the case of a girl under the age of consent, makes the procurement of even the solicited act of intercourse *legal rape,* as far as the male is concerned. This may apply, incidentally, whether or not the offending male is of age.

If anyone in the Pacific Northwest should have seen these unhappy patients it is myself. Through the courtesy of pediatricians and gynecologists alike, I have had the doubtful privilege of seeing a considerable number of the little girls in this large territory who have been involved in actual or suspected dealings of this sort. I am pleased to report to you (although perhaps for purposes of scientific study I should be sorry) that my actual observations are meager, which brings us to the patent observation that proved instances of actual rape or even the aggressive attempts during childhood are very rare indeed. The number of times that the accusation is made is another matter entirely and involves some considerations which I believe are of interest for discussion here.

I have mentioned "the age of consent" as demarcating that age under which any proved act of intercourse, whether it be by acquiescence or even by solicitation, may be construed as rape. Force, under this age, is not essential to the charge. In the state of Oregon the age of consent is 16 years. In the state of California the age of consent is 18 years. In a number of states it is as low as 14 years. Since complete delinquency in young girls and even frank prostitution is assumed frequently prior to the age of 18 years, it will at once be obvious that many peculiarities and difficulties are to be encountered in legal procedure in this category.

There are various legal interpretations of the term intercourse, but in most instances it implies that penetration has occurred. Absolute definition of the term penetration also involves legal complications which we cannot discuss here in further detail. I would like to note, however, perhaps rather obliquely, that actual penetration has been allowed legally to have occurred in the presence of an unruptured hymen. I know a number of such instances, and in one case in which I had to testify, penetration was legally allowed to have occurred in a girl of sixteen with an intact, if somewhat patulous, hymen. Over against this fact, I would like to call your attention to the frequent finding by any one who examines many minor females of a flat, adult, almost marital type of hymen in an unimpeachably virginal individual. Whether or not such a finding may be the result of masturbation or whatever other factor, its occurrence is not to be denied. I mention these factors merely as precautionary in relation to incautious statements and deductions in this exceedingly delicate bracket.

The usual examination to establish evidence of the act of rape in the immature female involves several components: First, one must inspect for bodily injury to the child elsewhere than in the genital area, caused by the forces required to subdue her. Such injury, incidentally, should always be present to satisfy the honest observer that the action involved is not by acquiescence or solicitation. The matter of acquiescence, or, as the court calls it, "consent," is of absolute importance in establishing the real guilt of the male, regardless of the fact that legally the questhe point that, in the case of children, the assignment of actual guilt is of vastly greater importance than the satisfaction of stupid legal technicalities. Again, one is apt to note local injury caused by strenuous attempts at preparation for the act; and finally, only very rarely indeed does one find actual injury caused directly by the male organ. It is obvious then, even where the history of attack is clear, that the demonstrable injury may seldom be expected to be typical. Efforts at actual penetration of the vagina, more often digital than penile, generally cause bruising, contusions, and lacerations of the external vulvar structures. The hymen is seldom, but occasionally, typically lacerated. These lacerations will appear as visible bleeding or raw linear splits. Further force will naturally penetrate the surrounding structures, generally the perineum, later the vaginal wall, occasionally resulting in complete tears of the perineum, tearing injury to the bladder or urethra, and other results of massive trauma. I shall not discuss this matter further here, since pediatricians will not be called upon to proceed far in such a case. I do wish, however, to clarify the matter a bit and to ask for your healthy skepticism regarding the alleged criminal background of so many of these cases.

I have noticed that physicians in general, and particularly specialists, are so much engrossed in the scientific aspects of these matters that they often fail adequately to consider their own interests and those of their patients from the social and medicolegal angles. Mr. Dan Northrup, of Portland, attorney for the Children's Division of the State Bureau of Health, and Mr. Walter Evans, Past Deputy District Attorney in the Portland Police Court, have for a number of years studied the authenticity of the accusations and disposal of cases of this sort which have come before the city and state authorities in Oregon. Their findings present a very sorry spectacle indeed. The first mistakes, which are very frequent indeed, are those made by the relatives of the injured child. The chief harmful components in these patterns are: (1) a morbid and overemotional response to the child's story, without real proof of guilt; (2) personal efforts to punish the alleged aggressor by physical means or by word of mouth; (3) early and ill-considered recourse to court procedure.

Unfortunately, also, frequent and damaging errors are too frequently made by the examining physician. These involve: (1) approval or even acquiescence in the ill-considered activities of the patient's family; (2) mistaken and damaging state-

ments based upon badly taken histories and misinterpreted physical findings; (3) actual participation of the physician in *any* legal proceedings. It becomes increasingly obvious to anyone who studies these matters with care that the physician must keep himself as clear as possible from any entanglement in the legal aspects of such a case. If he is willy-nilly drawn into court procedure, and even (I believe myself) if he appears likely to be, he should retain in his own interest a reputable attorney with as much specialized experience as possible. Any fee involved in such a procedure will constitute the most excellent insurance against its very serious potentialities. Time forbids any detailed consideration of these matters in this setting. Briefly, however, their importance can be indicated by condensed case reports picked from hundreds which exemplify such glaring errors.

Illustrating the distorted logic which may characterize the parents' story is the case of a fat and unprepossessing little girl of 7 years, who was brought to me for the treatment of a rather mild chronic nongonorrheal vaginitis. The mother stated categorically that the discharge was the result of sexual advances by an elderly man, a storekeeper in the family neighborhood. She stated that the child had been abused by the old man several times, and that other little girls in the neighborhood had been approached by him. She believed that the child had gonorrhea and wished to go to court at once. An unofficial investigation revealed that the old man in question was a friendly, perfectly harmless, and apparently perfectly decent storekeeper, very kindly to the children in the neighborhood. Nothing could be uncovered to substantiate the mother's story, and she subsequently denied that she had said that other children had been bothered. She could not name any, in any event. The child, on careful questioning, did not give a story which implicated the old man in any serious way, and any suspicious components in her story appeared to be highly colored by the mother's opinions. It subsequently developed there was a long-standing animosity between the mother and the storekeeper on the basis of an old unpaid account. The vaginitis was easily and completely cured. The mother was finally placated and the whole matter was dropped. I believe this unfortunate sequence can be laid directly to the mother's reading of half-baked pseudopsychiatric drivel in lay periodicals.

As exemplifying what may happen to a child when court procedure is invoked, there is the following case synopsis: A girl of 14 had apparently been initiated into various acts of sex perversion by her foster father. Under pressure by zealous relatives the child was first interrogated by the police. The matter was then taken to the district attorney where she was again cross-questioned at length. Finally, before the grand jury and again in public at a preliminary hearing and once more in the final trial under cross-examination, this child was required to recreate the sordid details of her tawdry experiences. After this she was put through a humiliating grilling by the defense attorney in an attempt to establish her complicity.

Suppose we omit a consideration of the justice of punishment of the offender in such a case and consider simply what the ordeal must have done to this child's sensitive and unstable psyche. It is quite impossible here to discuss the question of proper punishment of the offender. Suffice it to say that the hardships involved in any court procedure may, and often do, definitely outweigh the value to a community in obtaining a conviction. The efficiency and justice of penal measures in this bracket are sufficiently questionable. The psychic trauma suffered by a child under such circumstances may be beyond measure.

Now, as exemplifying the mistakes which may be made by the physicians, over and above their acquiescence in such mistaken notions as I have cited, may I give you a glaring example:

> A little girl of 5 years of age was brought to my office with an obvious fulminating gonorrheal vaginitis. It developed that the child had started to manipulate the genital area some months before. No genital examination had been done, but at about the same time a profuse vaginal discharge and irritation about the vulva had been noted by the mother, who concluded that this condition was secondary to the practice of masturbation. All manner of threats and dire punishments had failed to control the self-manipulation.
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> The child was taken to a physician who, after using external washes for two weeks, finally removed the child's clitoris. When she was seen by me, she had developed a postoperative scar contracture at the mouth of the urethra which made urination exceedingly difficult and painful. The vaginitis had not been diagnosed or treated up to this point. The child still manipulated her genitals. The vaginitis was easily cleared up and the urethral stricture relieved; the child immediately ceased self-manipulation, but remains sans clitoris. This is the reductio ad absurdum, and yet is a matter of established record.

Precocious Sexual Intercourse.—Before certain more general aspects of this matter are discussed, it may be well to consider also the general subject of precocious sexual intercourse. You, as pediatricians, will know more about the potentia of small boys than I do. Little enough is understood and little spoken about this matter, but certain fairly clear pronouncements emerge as far as young girls are concerned.

Fertility in the Child.—Dr. Sevringhaus will discuss the maturation process in the female. I would like to discuss it in relation to fertility in childhood and adolescence. I am inclined to agree with him or perhaps even go beyond him in the thought that the majority of early bleeding cycles in the majority of young girls are on an anovulatory basis. I have some patients with endometria which are of interest in this connection, and a number of astute observers are coming over to this concept. I mention this in the interest of the established fact that fertility in adolescence and beginning maturity is notoriously low. Even girls who appear to have established perfectly normal menstrual cycles are conspicuously infertile up to the average age of 18 years. In certain parts of India where cohabitation begins with the menarche, a child is seldom born before the third year of actual sex relations. In other races where coitus is unrestrained and frequently definitely aimed at the accomplishment of early pregnancy, such pregnancies are extremely rare. The inference seems reasonable, then, that on the female side there is considerable natural immunity during this period. I would welcome a statement from some one of you who will speak authoritatively in relation to the potentia of the immature male.

Precocious sex contacts or actual attempts or the performance of intercourse by children are matters which seem willy-nilly to intrude themselves for consideration. These considerations naturally include the rather common and frequently quite innocent carryings-on of unsupervised groups of children at play. No pediatrician will have avoided listening to the horrified parental recital of episodes involving playing at doctor and nurse; the business of sex cross examination; experimental efforts at giving enemas, douches, etc. These are pretty common elements in the careless institutional regime and not too infrequent among any children who are given considerable unsupervised playtime. Such seances, of course, may go on to abortive experiments at playing "papa and mama," and occasionally involve group

masturbation. These goings-on must be evaluated at their honest face value and in my experience are seldom as alarming as they appear to the outraged parents. The fact is, however, that they may easily create a background for more advanced sex experimentation and have often been the key factor in the dissemination of gonorrheal vaginitis in institutions.

Certain factors in our increasingly complex so-called civilization appear to exert a definite influence in the increasing frequency of precocious sex contacts. For myself, I am perfectly convinced that modern picture magazines, the curve-contour comics, and the superpassionate motion picture are sufficiently realistic to arouse and continue the embryonic libido of the newborn babe.

Granted these factors as chronic irritants in a situation already inviting a flare-up, we have only to add certain environmental factors present in many modern families to complete a picture of innuendo and actual example which the average child can hardly escape. Large families crowded into small quarters can have little secrecy even for their legitimate intimacies. The effect of alcohol on parental and, in fact, on total family inhibitions, including the children themselves, is not to be minimized. Considering the overdeveloped emphasis on sex in so much of our present-day living, it really seems rather amazing that children escape these sexy trends as often as they do.

Masturbation, which I will discuss later, goes pretty much hand in hand with most of the other precocious sex activities; that is to say, auto-acquaintance with erogenous areas is the most frequent prelude to the vicarious experiment. I think myself, that in the case of the child, a morbid curiosity and the desire to be out ahead of the pack more often accounts for intersexual activity than any true sexual drive. True enough, the inverterate masturbator is not apt to develop a strong interest in the opposite sex. For the majority, however, the whole matter is more or less tied up in the same bundle of half-developed impulses and curiosities.

The reasons that children seldom get beyond the experimental stage in these matters are numerous. In the first place, they are frightened; in the second place, they are not adequately equipped or prepared for successful consummation; and in the third place, they are seldom, if ever at all, in love. These rather simple and obvious factors account for the fact that little is accomplished except the satisfaction of a morbid curiosity, and in the case of the boys, at least, something acquired for adolescent boasting. For the true erotic type, much more is to be achieved by masturbation in this age bracket.

Masturbation.—I believe myself, as I am certain most of you do, that masturbation in a female child is chiefly a behavior problem, often of a rather simple sort—to be sure, seldom in the truly psychopathologic realm. From a gynecologic point of view, masturbation is of interest as resulting from local factors creating irritation and itching and resulting in manipulation which sometimes merely counteracts the local irritation, but more often also induces pleasurable and seductive sensations which invite repetition. The gynecologist may appropriately be called to deal with this situation in relation to its results as well as its causes; that is to say, local trauma of considerable proportions may be induced. Here, by the way, is a factor of definite importance which will be considered later in relation to medicolegal factors. Any child, but especially older children, may inflict considerable actual damage upon themselves at the height of the effort to achieve an orgasm. Friction often creates the appearance of an acute primary vulvitis. Invasion of the vagina may cause and maintain vaginitis. Physicians may occasionally find quite unexpected degrees of self-injury which may too easily be ascribed by a clever child or a morbid parent to injuries by a second party. If we envisage this possibility together with the occasional agency of irritating foci due to smegma or adhesions, eczema, or similar local conditions, we will not arrive at false conclusions or neglect to treat

the true underlying condition. However, it must not be supposed that the eradication of an original focus of irritation will in many instances cure an established habit of masturbation, which may continue under its own impetus.

There are no sound statistics to indicate at what age masturbation is most apt to begin in the female nor are statistics relative to its incidence reliable. By inference, many female children may be classed as masturbators, yet within the limits of such inference the practice may vary from simple vibratory mucosal stimulation, or scratching, to complicated attempts to simulate intercourse and achieve orgasm. Some authorities, stating that almost every female child masturbates, may not be overstating the case according to their own definition of the act. As long as these authorities are not trying to make us gasp in open-mouthed horror we are satisfied. The fact of the matter is that most of them, by propounding such statistics, are actually trying to establish a realization of the universality and harmlessness of the habit. We shall gain nothing, then, by attempting to argue the point.

Infants under 1 year of age have been known to manipulate the genital area habitually. This activity, definitely on a par with thumbsucking and nailbiting, should doubtless be regarded with more concern at that point in its development where it achieves or seeks to achieve an orgasm. In fact, from the point of view of its social effect, any such practice in an older child is to be regarded more seriously because it exists in an environment of adult patterns. And here lies a sort of paradox; psychologists and psychiatrists insist that the habit of masturbation in older children and adults is less harmful where it holds a mental image of actual performance—at least a working concept of the opposite sex. Common sense, on the other hand, seems to indicate clearly that the performance of masturbation by children as a psychic substitute for the sex act should certainly increase the trend toward premarital indulgence. It is all very mixed up. I certainly do not know the answers.

To discuss adequately the clinical and social aspects of this problem, we should present case material in at least four different categories representing the various grades of masturbatory involvement in the order of their seriousness. Such a discussion, in extenso, is, of course, impossible at this time. Briefly, however, the types may be characterized as follows:

> (1) There is the entirely normal, healthy little girl who itches about the clitoris or who is conscious of some mucosal response in this area, and who therefore teeters over the edges of chairs, applies her finger or her bedclothes to the genital area and embarrasses her parents and attendants but not herself. The habit is about on a par with a facial tic as far as its real connotations go. (2) There is the spoiled, pretty, and rather sensuous child of overindulgent parents who enjoys masturbation rather deeply, is ashamed of the habit, but unable to control it, once started, even under the danger of detection. (3) There is the repressed, overdisciplined, unhappy child of aggressive parents who finds masturbation the best solace for her solitude; this is a grim and unhappy child whose prognosis is bad because she is unapproachable. (4) There is a natural or potential delinquent—a handsome, stupid, and lethargic, but sensuous type, with little or no conscience; this child is not frightened, is acquiescent to males, and is impressed by promises of immediate rewards. She is frequently involved in clandestine meetings with older boys. She masturbates methodically and without shame or fear. She is fertile soil for venereal disease and is a potential prostitute.

The prognosis in these four empiric categories varies all the way from good to bad. The impulse to ride with the psychiatrists for fine flights of fancy grasps us all at

this point in our consideration of the problem. Incidentally, concerning this matter of masturbation, I am relieved to find that most pediatricians do not feel themselves any better equipped or more adequately informed than do most gynecologists. Some psychiatrists, on the other hand, rather fancy their commitments and write prolifically. Unfortunately, most of their writing follows the form of case analysis, almost entirely fashioned on the subjective reactions and isolated thoughts of the individual psychiatrist. It seems to me that the pseudosex systems of superpsychiatry in this field, which have developed chiefly in this way, hold glamor chiefly for the so-called social hygienist whose scientific grounding is shallow. I have gone quite a long way with these people in the attempt to achieve their conviction of knowledge in this field. I am forced now to believe that where their ideology leaves the plane of ordinary logic and wanders off along peculiar paths, to the utter confusion of the average intelligence, those of us who claim no more than an average intelligence have a right to an attitude of healthy skepticism. I believe that the simpler methods advocated by most child psychologists and the plain methods used by most pediatricians in their everyday practice are considerably more valid.

Strange how easy it would seem to conclude a discussion of masturbation in female children without a section on treatment. Consecutive thinking in the matter seems to end, somehow, quite abruptly at the point where aggressive therapy begins. The reason may be that the best treatment of masturbation is more on the passive than the active side. Radical measures, either physical or psychologic, are certainly contraindicated. Severe physical punishment, drastic disciplinary measures, heavy religious and moralistic exactions, and above all, the invocation of the doctrine of fear, are not sound—none of them. Local foci of irritation, uncleanliness, improper clothing, and the like will be dealt with easily. The child's confidence and sympathy are to be cultivated to the utmost. If her own thought can be elicited and her interest aroused in an intelligent plan of treatment of her own, valuable ground will have been gained. Rewards may be of value but should be tangible. A row of stars, for example, on a blue chart on the wall above the child's bed is not apt to serve the purpose as well as a valued gift or a real honest-to-goodness treat. If the affectionate will of the child to cooperate can be stimulated by palpable rewards or in any other way, the most will be accomplished.

It seems quite as important to correct vicarious unhappy and noxious environmental influences as to attempt to eliminate the specific factors suspected as directly responsible. By this I mean that the child's antisocial activities may be triggered by some quite remote psychologic irritant. A complete study of the environment with, if possible, a change to healthier and happier surroundings; the instigation of sound new interests and ambitions; the effort to re-establish the child's self-esteem and to install her more happily among her companions—all such factors may be helpful in a program which must be extremely labile.

That there is so little written on treatment which is of practical value in the individual case does not indicate that the outlook for these children is consistently or even frequently bad. One has only to contemplate the actual outcome of the great majority of these cases to come over to the optimistic side. To have watched a sufficient number of children work through the mildly abnormal phases of the habit is to convince the honest observer that masturbation is as often noxious and harmful to the child's family and friends as to the child herself. If she does not conquer it in early life, she will in all but the rare instance have sufficiently controlled it by adolescence. I am convinced that the exaggerated instance involves psychopathic factors, not true components of the habit itself. The correct concept is something similar to that which is now broadly applied to alcoholism. The child is a psychopath and therefore masturbates uncontrollably, not the child masturbates uncontrollably and therefore becomes a psychopath. In any event, these more involved considerations are really for our more erudite friends, the psychiatrists.

It is hardly fair to let this matter go without admitting to you that I am perhaps a bit old-fashioned in my general concepts of its management. I believe that the too, too broad-minded, present-day attitude in such matters may have reached the peak of its usefulness and that a revaluation of physiologic and biologic actualities may not fairly be looked upon with lofty disapproval. It is quite all right to admit the harmlessness and the amusing qualities of the performances of the monkey at the zoo, but I do think that we are scarcely called upon to reserve the same sort of a perch for our own children and those of our patients. I do not choose, then, to dismiss the entire matter as inconsequential, nor am I willing to grant the argument of our long-haired savants that there is any advantage to the habit over abstinence from it. I regard the practice as harmful in the sense that it is a rather maudlin self-indulgence. I grant that if it is actually harmful, it is generally so in direct proportion to the emotional factors of fear and shame which are built up around it by misguided parents and physicians, but I believe that it exerts unhealthy influences upon the child's self-control and that the promulgation of the habit in others is equally undesirable. I believe that there is a definitely favorable influence in the healthy example of others, and in a well-ordered disciplinary regime, and in the temperate application of religious and rational moralistic programs.

The Contribution of Social Service.—Now, I would like to discuss with you rather candidly some of the errors and some of the conspicuous contributions which social service organizations have developed in connection with these sex deviations in children. First, let me say that if pediatricians are not aware of the solid assistance to be gained from such agencies, they had best inform themselves. Various independent agencies, either sectarian or under foundation endowment, are available in almost any community. County, state, and federal agencies have in recent years gone far beyond the unenlightened hide-bound legal grist-mills of the old days. We now have, in many of the child welfare agencies and juvenile courts, exceedingly sensitive, intelligent, and personalized organizations. Too much cannot be said in praise of the influence of the federal government under the Department of Labor in sponsoring and maintaining this excellent trend. Unfortunately, physicians as a whole are not sufficiently aware of the intelligent and effective forces now available for assistance in these problems.

Criticism may occasionally justly be leveled at the individual social workers whose undercover interests may be (1) the creation and maintenance of a well-paying easy job; (2) the opportunity to ride a hobby; (3) a long-nosed, morbid curiosity about other people's intimacies. Under the first heading we may cite the overzealous activities of some of the endowed foundations—the "wheels within wheels" type of organization which is self-perpetuating in the interests of the individuals who live upon the endowment. Illustrating the second group there are those who use and misuse their strategic situations in the interest of hobbies, religious or social. Putting aside the major issues, which are obvious, you as pediatricians will not have escaped the recently supervised crusade by social workers to have circumcisions done upon all little girls suspected of any sort of vulvar irrgularity. The procedure had become in the minds of a good many zealots a cure-all. This is the type of hobby which may occasionally be ridden to death by a few social service cranks. It is hardly necessary to characterize for you the type of social worker whose warped interest centers definitely in the tainted personal aspects of these problems. To be sure, this type of individual is not often employed by reputable agencies and is by necessity now-a-days more restrained in the pursuit of her peculiar interests. Existing agencies are to be congratulated upon spotting this trend and smoking out its exponents. There is no place in a social service organization for an individual who sublimates his or her own distorted libido in the contemplation of the sordid sexual toils of others.

In the conduct of sex deviations involving infants and young girls, an absolute knowledge of the child's environment, an honest analysis of those who affect the child directly, and a personal study of all of the individuals directly and indirectly involved in the incident are matters of absolute value. To procure these data requires the services of a trained case worker. The average physician will find himself ill-equipped in this field and will, in any event, not be able to devote the necessary time. The services of reputable agencies are therefore routinely required, and physicians must acquaint themselves with the resources available in their individual localities.

It is unfortunate that such agencies are devoted almost exclusively to work in the charity bracket. It seems too bad that for individuals who are able to pay all or part of the expense the only available service is by an irregular arrangement with the charity and governmental agencies. In a few of the larger cities social service case workers may be employed by private physicians or private families in this interest. Such an arrangement, however, cannot usually be made. The psychiatrist, of course, in private practice may be equipped to deal adequately with such matters, but again he, too frequently, is not backed by a case-finding organization and has neither the time nor energy to get to the roots of the matter himself. Here is a situation which demands our interest and in which I should think an organization such as yours might take a very intelligent and very effective interest. The lack of available case-finding agencies for reference by private physicians is a definite flaw in our machinery.

Pelvic Examination of the Adolescent Girl

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For many years I have felt very keenly that the answer to many of the most important problems that we, as gynecologists, are confronted with in daily practice can be adequately answered only by thorough and persistent training of the adolescent girl. It has seemed that this can be accomplished best by proper training of the doctor and through him the parents, particularly the mother.

It is undoubtedly true that the other branches of medicine, including gynecology and obstetrics, have, for the most part, sadly neglected or avoided this great field of preventive medicine. You, as pediatricians, are to be congratulated for assuming the additional responsibilities of the period between childhood and maturity. A perusal of your proceedings suggests that it has been done with a certain feeling of resignation rather than as a challenge to compensate for our shameful neglect of the teen-age girl in the past. Dr. Graeme Mitchell[1] epitomized this feeling recently when he said, "We may need the endocrinologist from time to time, the gynecologist and the educator, in a cooperative job with the pediatrician as a guide, and certainly we can no longer refuse to give our assistance, our knowledge with our background to the child who is over twelve years of age. That is, the adolescent belongs to us."

Relatively few gynecologists and obstetricians have interested and perfected themselves in methods of examination to include this vitally important part of medicine. In the dispensary, the pediatric hospital, and in private practice the little girl who had passed the age of pediatric care was, and unfortunately often still is, a much neglected individual. Until she reaches the premarital or adult stage only serious anatomical lesions of the pelvis or those of venereal taint seemed to warrant proper scientific or serious study. The far greater group of anatomic, physiologic, or psychologic aberrations were either disregarded or left to nature, parents, church, or school to cope with.

I firmly believe that a combined program conducted by the mother, the pediatrician, and the gynecologist or obstetrician will do more to promote the health and happiness of the child and to prevent later disease and death in the woman than

any of our current programs of prenatal care. It would seem reasonable that the obstetrician-gynecologist should be included in this triad. He and the pediatrician should occupy a peculiarly intimate position in the respect and, I hope, affection of the mothers of this country. Our advance in this program of education and study of the pelvic problems of the little girl and the adolescent will be in direct proportion to our influence in the education of her mother.

Our first effort must therefore be during the prenatal and postnatal period to imbue the expectant mother with the idea that a regular complete physical examination will do more to assure her and her daughter of health and happiness than any other form of life assurance that she can buy.

Second, these examinations should be at regular intervals, at least yearly and preferably each six months.

Third, and of the utmost importance, the training of doctors so that when a patient comes for examination it shall be thorough and complete, even in the absence of symptoms. Our programs of preventive medicine and cancer control have failed to a large degree because we have taught both our patients and doctors to wait for symptoms rather than to find lesions and treat them early enough to effect cure. We have waited for the tooth to decay instead of saving it by the prophylaxis of early repair.

Adair[2] asks in a recent symposium on gynecologic cancer, "How is the woman to be brought to the doctor? Should she be educated to have periodic health examinations or to seek medical advice upon the appearance of certain signs and symptoms or both?" The rising death rate from cancer, I think, indicates education in both principles. Thirty-six thousand, four hundred twelve deaths from cancer of the genitals and breast in women during 1940 is a staggering figure. Forty-four per cent of all cancer deaths in women are due to cancer of the genitals and breasts. A woman's dislike and dread of examination of these systems is largely responsible for this terrific toll and dates back to her adolescent training. If we add to this disgraceful situation the dyspareunia, frigidity, sterility, malformations, infantilism, fear of pregnancy, illegitimacy, dysmenorrhea, postabortal infections, etc., which we see almost daily in routine practice, a change in educational procedures becomes imperative.

You, as pediatricians, have done a splendid job of prophylactic medicine in encouraging mothers to bring their children for vaccination and immunization, care of the eyes, teeth, nutrition and heart. I am afraid that far less emphasis has been placed both in teaching and in prophylactic treatment of the examination of the female genitals which will be the site of approximately 30 per cent of the patients' future ills. I am sure that you will not fail us. When we turn over to you our girl babies at birth, we ask that you continue the education of the mother in the importance of routine inspection or examination of her daughter's genitals, that the growing youngster under your direction comes naturally to accept this as a part of her routine physical examination. We ask that you offer in your pediatric curricula a cooperative opportunity for training of future doctors in the problems of the adolescent: that when special problems of treatment or diagnosis arise that you allow us to cooperate with you in further study of these vitally important problems and to help with the rounded-out education of this future mother. We insist that you join us in a scientific program of conditioning the child for medical care in this field as adequate as that which you yourselves have pioneered in so many other fields of pediatric practice.

Adult patients, speaking in retrospect, have firmly convinced me that we need to go back with our education into adolescence or before in order to secure the optimum results in this field of preventive medicine. It is very difficult for us to change a blonde to a brunette at the age of 20 years. A patient who has never had a pelvic

examination until this late date will avoid one at all costs for the rest of her life whenever possible. When doctors and parents alike have averted their eyes and pulled up the sheet over that area between the navel and the knees for twenty years, it is ofttimes difficult for us to get even minimum exposure for an adequate pelvic examination. Even under the deepest anesthesia the patient will protect through shear habit with her hands and thighs that portion of her anatomy which she has been taught to keep inviolate at all costs.

Frank[3] recently said: "Today we are realizing that the adolescent is the forgotten child about whom little is known and for whom little systematic care is being provided. Because we have focused our attention previously upon the specific event of puberty, such as the menacme, these highly important developmental and maturational processes in the preceding years have either been neglected or ignored. At this period rapid developmental changes are taking place in the skeleton, in the gonads, and in the reproductive organs that are of considerable significance in the individual's health and normal functioning."

Shorr[4] believes that "the chief aim of therapy should be to prevent extreme deviations within a given type. That, by sane control of environmental factors, we will permit the optimum development of the potentialities of the individual." This author feels that most of the endocrine problems of adolescence are expressions of physiologic variations which can best be handled by a sane program of physical and mental hygiene.

Two years ago Sevringhaus[5] stated that as a new point of departure in education we medical women and men can point out to girls, to parents, and to teachers alike that the secondary sex characteristics both physical and psychological are integral parts of the hormonal-conditioned development of the person. I am very certain that with the advance in our knowledge, we will be able soon to prevent many of the minor, as well as the pronounced, deviations in physiology.

If mothers had been educated to spend even half the energy in frank, intelligent discussion with her curious daughter on the problems of sex and the physiology of her pelvic organs that she squandered in crowding spinach down her protesting offspring, a valuable start in these problems would have been made. Supplemental, even if time-consuming, understanding discussion by the doctor with the child and the mother should cover those angles which the adolescent hesitates to discuss with her parents, and often the mother must be excluded to insure any effective contact with the child's independent thought process. I do not believe we need fear stimulating a premature or abnormal interest in these matters of sex by honest discussion. The prime interest of these healthy young animals is sex and matters pertaining to it. Lack of interest on their part in these matters either denotes hypofunction, parental dominance, or physical disease. Our duty is an honest, unashamed discussion upon which the child's judgments may be founded.*

I disagree with Baer when he says adolescence in the healthy girl whose home life, school life, and social life are normal requires little or no medical attention. In this period of tremendous increase of drive, unstability, and uncertainty, what child will fill this bill? What little girl do any of you know that would not welcome the knowledge that she is normal and have given to her an honest explanation of what her problems mean and help in meeting them? I believe as our attitudes change and our methods become perfected, every individual will be accorded the benefit of a careful complete physical examination at routine intervals so that efforts directed toward correction may be instituted early before irreversible changes have occurred. Frank has noted that the evidence of physical defects and handicaps among draftees may also be cited as indicating the neglect of adolescents.

*Mohr believes that there is no information having to do with normal sexual relationships, conception, and childbirth that we need withhold from an adolescent. More careful planning of our consultation time will permit us to impart this information to the child and her mother more effectively.

One interesting but pertinent sidelight in this connection is the difference in army requirements for physical examination of females for active service. I am not sure whether it is founded on social standing or just a matter of rank. The W.A.A.C's who will probably only see homeland service are required to have pelvic examinations. The nurses, many of whom will see foreign service, are not. Many mistakes in differential diagnosis of pelvic problems in the adolescent are founded on the same basis. When I recently asked the commanding medical officer of a large hospital unit if he did not think he was assuming a great responsibility in taking 120 nurses to the Egyptian desert without previous pelvic examination, his answer was enlightening. His first response was, "Why should they have?" and later, that he did not believe that the girls would permit it. They are now receiving their pelvic checkup without any fuss or feathers. In fact, many of them have expressed relief and satisfaction when they were assured that the findings were normal. Some major and many minor lesions are now being corrected which would otherwise have passed unnoted. In three hours of examinations in forty-eight women applying for service with the W.A.A.C's, five fibromyomas as large as an orange or larger were found. A cervical cancer was present in one applicant. Two large ovarian cysts and two endometria of major proportions were also discovered. The required physical examinations for this war emergency may give great impetus to our conception of the advisability of complete physical examination of supposedly normal women and will point to the need of even earlier attention. Females should be trained early not only to expect this but to demand it.

Even the simple rules of an adequate pelvic examination in the adult woman have not been mastered by a large percentage of the medical profession. Women regularly dread and avoid these procedures due to the bungling methods of an inept examiner. She is not apt willingly to subject her daughter of tender age to such procedures. On the other hand, if her own experience has been expertly handled with a minimum of discomfort, she will much more readily consent to it for her daughter. Mothers have volunteered this information many times.

The gross gynecologic diseases of the adolescent girl have been quite adequately studied and discussed. Baer,[6] in a splendid paper for your symposium of two years ago, clearly outlined the diagnosis and treatment of these conditions. In spite of this present knowledge many grave errors in diagnosis and treatment are coming to light daily. May I only cite some of those cases that we as gynecologists are too frequently confronted with? Imperforate hymen, rigid hymenal rings that wreck marriage in the first twenty-four hours, absence of the vagina, septate vagina, pelvic tumors, menorrhagia, prolonged amenorrhea, severe dysmenorrhea, vaginitis hermaphroditism, functionless breasts, inverted nipples, marked pelvic infantilism, foreign bodies, etc.

It would seem to me that our future problem is to extend our observations and studies to include also the larger group of borderline pathology just as we have done in the fields of vitamins. We must bring to this field a scientific attitude unhampered by the father-daughter, brother-sister complexes which have made the intact hymenal ring an insuperable barrier to the study and advance which the great importance of this field warrants.

Therefore, asking your indulgence, I should like to discuss and illustrate briefly some of the points we think are important in the routine pelvic examination of the adolescent girl—that the patient be conditioned by you and her mother from infancy forward to accept pelvic inspection or examination as a part of routine physical examination. This pelvic examination must be more inclusive in its scope as the child grows. The preliminary steps should include careful inspection of the external genitals. Subsequently, before puberty, applicator or probe investigation of the patency of the tract and recto-abdominal palpation to discover early minor or gross

deviations from the normal. We believe that a child can be taught to accept a pelvic examination with as little fuss as an examination of her tonsils. There is no gagging reflex associated with pelvic investigation. At some time during the late adolescent period a complete pelvic examination including visualization of the vaginal canal and the cervix should be done. In most instances this can be accomplished without difficulty by instrumentation and rectovaginal examination. Hymenal rings that are too tight to permit this have wrecked more marriages than they have saved indiscretions. Inadequate drainage anywhere in the body predisposes to infection. If we are agreed as to the advisability of examination in the adult, we should not deny it to the younger sister.

My experience has been that the knee chest position offers many advantages over the recumbent position. The parts are more readily exposed. Better control of the movement of the patient can be maintained and instruments can be more steadily and therefore more gently manipulated. Anesthesia is rarely needed but should be resorted to without hesitation. Ethylene anesthetic has been most effective in our hands. When anesthesia is required, the need for examination becomes correspondingly more imperative.

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Infections of the Immature Female Genital Tract

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This symposium has been arranged largely through the recognition of the importance to pediatricians of a further knowledge of the immature female genital system and its disorders. We have considered the adolescent period a "no man's land," and it is only relatively recently that we have taken sufficient interest in that period to attempt to learn something about it. In similar manner, we have somehow felt that dealing with genital disorders in girls was outside our field. To a considerable extent, the gynecologists have also shunned the field, partly because of a lack of knowledge, and partly because they have not become proficient in the examination of infants and young girls. I believe a great deal can always be gained by a discussion in a field in which two specialties should be interested and mutually assume responsibility. It must be admitted that the field has been shamefully neglected in the past. There is much to be learned and much that we pediatricians can contribute to the field. There is nothing new presented here, but I shall review with you some of the fundamentals around which we are now basing our treatment of infections in the immature genital tract.

Anatomy.—There are certain fundamental anatomical differences between the immature and adult genitals in relation to infection. The immature genitals show an increased vertical axis; the vulva are more anterior; protection pads are thinner; the vaginal orifice is less recessive; there is no protection from pubic hair; and the rectum is closer by actual distance. All these considerations, plus the fact that immature girls are more active, more careless in their habits, and worry less about cleanliness, should lead to greater possibilities of infection. A comparative gross and microscopic study will show certain differences, which may account for the relative frequency of infection in certain parts of the genital tract and relative infrequency in other parts.

The Bartholin glands show a very simple glandular structure with a rudimentary glandular epithelium in the immature female. Clinically, they are rarely involved

even in the most severe of gonorrheal infections, so are of little importance in our discussion.

The immature urethra is lined in its anterior two thirds by stratified squamous epithelium, and in its posterior third it gradually merges into a transitional type of epithelium which is also seen in the bladder mucosa. Emptying on each side of the urethra at a point near the meatus are the ducts of Skene's glands. Scattered irregularly back to the bladder neck are smaller mucous glands, which may be considered analagous to the glands of Littre in the male urethra. Glandular structure here may be complex, but it is characteristically rudimentary and undifferentiated in cell type. For this reason, the urethra is rarely considered as a source of infection for the vagina. Urethritis, on the other hand, may occasionally result from extension of vaginal infection. Skene's glands may harbor the gonococcus, but the occurrence is rare.

Concerning the Vagina.—In a bloc sagittal section through the genitals of a female stillborn at term, certain important characteristics of the immature vagina and vaginal cervix may be demonstrated. The vaginal cavity is a potential cavity only. The fluted and cryptic walls are closely approximated, and considerable positive pressure is required to force the walls apart. There are characteristic longitudinal plicae of the lower portion of the vagina and the more circular pleats of the upper portion. The tight hymenal orifice together with these deep crypts and a rather static serous secretion make an ideal harbor for infection. It will also be noted that the vaginal cervix is rugose in character. It is interesting to observe that the vaginal cervix and the endocervix reverse roles as sources of infection in the child and the adult. In a low-power sagittal block from a stillborn infant the lack of cervical glands and the rudimentary nature of the endometrium may be noted. Under higher power the cryptiform conformation of the vaginal cervix and the almost complete absence of endocervical glandular structures may be seen. The rudimentary nature of the cervical gland structures often persists up to the fifteenth year. Schauffler's experiments in injecting opaque material into the vagina show that the vagina filled well, but in no case did the x-ray show penetration of the material into the cervical canal. These factors no doubt contribute a relative immunity of the child to gonorrheal pelvic inflammatory disease.

The vaginal epithelium presents a very interesting picture in relationship to vaginal infection. The epithelial layer is relatively thin during childhood as compared to the mature vaginal mucosa. Due to estrogen activity in the mother, the newborn female vaginal epithelium is relatively thick. The superficial layers slough rather rapidly. This accounts, in part, at least, for the grayish vaginal discharge often noted in the newborn period. It has been well demonstrated that the thin epithelium of the young girl is an ideal harbor for the gonococcus. The thickening of the mucosa during estrogen therapy accounts for the increase in the mechanical protection against the gonococcus. Squamous epithelium not only covers the vaginal cervix, but may persist well within the cervical canal. That fact, plus the very rudimentary glandular structure of the endocervix, strongly points toward the fact that neither infection nor reinfection of the vagina occurs from this area.

The biochemical reaction of the vagina is an important factor in relation to vaginitis. By means of indicators such as nitrazine paper (Squibb), the hydrogen-ion concentration can be determined relatively easily. This gives us a practical method by which to determine progress of treatment. The normal hydrogen-ion concentration of the immature vagina is neutral or faintly alkaline (pH, 7.0 to 7.2). This is apparently contingent on the breakdown of the glycogen present in the epithelial cells and released by their destruction. With the resultant formation of lactic acid, the vaginal pH decreases. It has been shown in vitro that the gonococcus grows best in a slightly alkaline medium. If the pH exceeds 6.0, the culture rarely survives. On this basis, Lewis theorized that the use of estrogens,

with the increase in epithelization and rapid breakdown producing lactic acid from glycogen, caused a rapid decrease in vaginal pH, and thus tended to destroy the gonococcus.

Variations occur in those factors which control vaginal bacterial growth during the normal life cycle and during pathologic states. The height of the mucosal cell layers, the glycogen content of the cells, the acidity (pH) of the vaginal secretion, and the growth of normal bacilli all vary in direct proportion from birth to senility and with various types and degrees of vaginitis. Prior to adolescence, specific vulvovaginitis produces a deficiency in these essential factors in proportion to the virulence of the infection. During pregnancy there is an increase in all these vaginal factors. After menopause the vaginal mucosa reverts to the preadolescent state with a corresponding reduction in all four characteristics as senile vaginitis develops.

Vaginitis as a clinical entity in girls has long been recognized and feared. It is not within the scope of my discussion to call attention to the social implications. The sources of vaginal infection may be quite vague. It has long been thought that toilet seats, bed linen, and clothing were potential sources. Careful work has yielded rather negative results where these items were concerned, even to the point of allowing noninfected girls to occupy the same toilet seats as those infected with gonorrheal vaginitis. Cohn and Carpenter found there was no cross infection. The frequency of spread in institutions, however, leaves little doubt that there must be an infective factor. Certain infections in the newborn infant have been traced to an infected mother, though vaginal involvement from this source is rarer than one might expect. The fact that some children, long thought cured, have been shown to harbor the infection has led to the supposition that there might be a carrier state. The fact that we are not sure of the source leads us to urge that extreme care and cleanliness be observed lest cross infection might occur. The rectum and urethra cannot be ruled out as possible sources of infection.

Nongonorrheal vaginitis is a definite entity and should be mentioned. There are some instances where gonorrheal infection is certainly to be suspected, but diagnosis is not established. Improvement in cultural methods may lead to a more positive diagnosis in some of these. Colon bacillus, pneumococcus, streptococcus, and diphtheria bacillus have all been suspected. Diphtheria, with membrane, has been demonstrated occasionally. Pneumococcus has also been implicated. The trichomonas must not be overlooked, but it is a much less common invader in girls than in adults. Any treatment which will reduce the hydrogen-ion concentration in the vagina should be very effective against the trichomonas. Rarely pinworms may migrate across from the rectum and cause a nonspecific vaginitis. The occurrence in the intestinal tract should lead one to suspect such a source.

We are not infrequently confronted with a history of vaginal discharge presented by the mother. Physical examination may reveal very little. If one is unable to detect any vaginal discharge, it is wise to instruct the mother to bring in the unwashed undergarments. A hint as to the reality and the amount of discharge may thus be obtained. Often a mild discharge will yield to simple hygienic measures. In such a situation, it is not necessary for the physician to proceed with spreads or cultures in the attempt to diagnose a gonorrheal infection. If, however, the discharge is persistent and does not yield to simple treatment, a careful bacteriologic study should always be made.

If a bloody vaginal discharge is noted, careful search for trauma should be made. Usually there is a more or less definite history, and some physical evidence is noted. However, many times trauma does not enter the picture. In such a case, foreign body should be suspected. It is probable that most of us have had an opportunity to visualize foreign body by means of fluoroscopic examination. With proper equipment for examination, it should not be difficult to determine whether a visualized foreign body is in the rectum or the vagina. Certain young

children seem prone to poke foreign bodies into their external orifices. The mother is seldom aware of the practice and is likely to be quite horrified if the child places something in the vagina. I fail to see any special psychiatric or sexual implication in the great majority of cases in young girls.

The bacteriology of the vagina presents some interesting features in the differential diagnosis of vaginitis. The vagina has been shown to be free of all bacteria until a few hours after birth. (Cocci appear first, together with gram-negative rods and *Bacillus bifidus* and *B. pipolaris*. A luxurious growth appears by the second day.) Döderlein's bacilli then appear by the fourth to sixth day. According to Dobszay, they usually disappear by the fourteenth day. He feels that their presence is always conditioned by maternal estrogenic influence on the infant vagina. Döderlein's bacilli do appear throughout childhood, and while they frequently appear after estrogen therapy, this is by no means always true. They cannot, therefore, be used as a reliable index of endocrine therapy. Their presence usually is accompanied by an increase in the glycogen level in the vagina.

Gonorrheal vaginitis can be diagnosed in several ways. By far the most common method is by spreads. This method is probably 50 per cent less accurate than cultures. With the improvement in the methods of culturing the gonococcus, it is urged that no questionable case be stigmatized without a positive culture. Whether culture or spread is used, the material should be taken well up in the vaginal vault, and not from the vulva. In examining spreads from immature vaginal tracts, a few differences from the adult are noted. The normal infantile vagina usually shows few or no pus cells. In younger children, if the döderlein bacillus is present, it is a good sign, for it should indicate that the pH is relatively too high for growth of the gonococcus. It is not within the scope of this discussion to detail methods of recognizing the gonococcus. Suffice to say that extreme care should be taken in the diagnosis, especially in the borderline cases. Clinical laboratories and especially the average city and state health offices are not always a reliable source of proper diagnosis. I feel that the physician should be thoroughly familiar with the spread as it applies to his individual case. Then, too, if the study is made at the time, a culture may be taken, thus saving time and doubt. Unfortunately, the facilities for taking proper cultures are much too rare. Technicians trained in proper technique, and especially in the recognition of the gonococcus colonies as opposed to others in the genus Neisseriae, are very scarce. A concerted effort on the part of the pediatricians and the gynecologists may result in the proper training of more of these technicians.

The *treatment* of gonorrheal vaginitis has been almost completely revolutionized since the introduction of the sulfonamides. With the introduction of sulfathiazole, a vast improvement over the results with sulfanilamide and sulfapyradine was noted. Whether sulfadiazine will be favored over sulfathiazole remains for further statistical study. Certainly both are relatively nontoxic, and it is now generally accepted that either may be administered without recourse to hospitalization. The use of sulfonamides probably will be most popular and most practical with pediatricians, as it obviates the need for vaginal manipulation. Certainly, if reliable results can be obtained without such manipulation, the treatment will be much less arduous both for the physician, the patient, and the family. Cohn and his associates have rendered a service in pointing out that, with adequate hygienic measures, 75 per cent of his patients with proved cases of gonorrheal vaginitis recovered in six months or less without treatment. He reasons that, if any series reports less than 75 per cent cures by any given method, that method should be discarded. He is probably right.

The older methods of instillation of ointments, the most effective being silver nitrate ointment, were considered quite effective. The ironing out by distention of the vaginal crypts, and even the distention by stretching through the rectum, seemed to effect some benefit. The use of other drugs by instillation, the cold

quartz light, and irrigations all had their proponents. Fever has been advocated by some, but this method is never completely without danger. Thus, estrogen therapy and sulfonamide therapy are now the methods of choice.

We have already discussed the physiologic effects of estrogen on the immature vaginal mucosa. Estrogen may be introduced by injection, by pellet into the skin, or by vaginal route with suppository. The latter method seems preferable from the standpoint that it combines the advantage of estrogen with the advantage of local distention of the crypts. In the introduction of the suppository, hymenectomy may occasionally be advisable. It should be inserted at night, after the child is reclining in bed. Care should be taken to introduce it completely to the vault. Liberal use of lubricating jelly is essential. The average parent can be taught to introduce the suppository by means of a long straight forceps. The estrogen should be applied each evening until the vaginal pH is 6.0 or less, determined by means of nitrazene paper. The vaginal changes, noted by the change in character of the vaginal spread, will determine the progress of treatment. The cellular changes, usually occurring from the seventh to the fifteenth day, ordinarily coincide with the disappearance of demonstrable gonococci. It is then safe to reduce to one suppository every other night. This should be continued from two to three weeks to play safe. If the treatment is not successful within a month to six weeks, it should be abandoned for another form.

A great deal has been said about the possible dangers of treating young girls with estrogens. From the standpoint of the vaginal mucosa, it rapidly returns to normal after treatment is stopped. Other effects, such as mild breast engorgement and sparse pubic hair, may occur. These also are temporary. I believe, however, that we must be very cautious in our evaluation of the possible dangerous effects of estrogen. It is possible that even a temporary stimulation may lead to a glandular imbalance of which we are not at present aware.

Concerning the sulfonamides, sulfanilamide has been quite completely discarded as being relatively ineffective, and also more toxic in effect. Sulfapyradine also has been discarded as being quite ineffective and relatively toxic. We all know that the vast majority of infants and children tolerate sulfathiazole very well. A few who get unpleasant side reaction, such as vomiting, from sulfathiazole can often take sulfadiazine. As far as is known at present, the latter seems to be about as effective as the former. The dosage is about the same as for any other condition elsewhere of mild severity. One-half grain per pound of body weight can be considered maximum. If in doubt, blood levels can be taken and maintained at about 6 to 8 mg. I feel it is advisable to start the dosage every four hours through the night for the first two days, then cut to five, then four, and hold on four for ten more days. Because of the fact that the organisms may disappear rather rapidly under sulfa medication, it is not advisable to stop when the organisms seem to disappear, as a carrier condition, or a flare-up, may occur. I feel personally that there is no objection to continuing medication for a much longer period if the case seems refractory or if there is possibility of reinfection. If the child is going to show sensitivity to the drug, it will be manifested in the vast majority of cases in the first few days of treatment. By watching the blood picture rather closely during and just after treatment, little danger can be encountered. The use of sulfathiazole vaginally in powder or jelly may offer considerable promise as it has done elsewhere locally. Results are awaited. The newer sulfonamides offer over 90 per cent cures, which is better than can be said of any other treatment, and it is my feeling that it will eventually supplant all other forms to a large extent. In a case which does not respond after a fair trial with sulfonamides, estrogen therapy should be tried. Foreign body must also be ruled out. The criteria for cure of vaginitis are important. The majority of workers regard a time limit of from three to five weeks free from symptoms, with three or more negative cultures (the patient not being under treatment), as satisfactory evidence of cure. There

are exceptions, and the child should be watched. She probably ceases to be a source of active infection, however, if the above criteria are adhered to.

Primary pelvic inflammatory disease in the young girl is apparently an exceedingly rare condition. Difficulties in making an accurate diagnosis of this condition render statistics concerning its occurrence quite valueless. It has, however, been demonstrated that the pneumococcus and the gonococcus at least have migrated up through the immature genital tract into the pelvic cavity. The relative absence of glandular elements in the endocervix, together with the narrowness of the endometrial and the tubal cavities, make the incidence of infection rare indeed. This is especially true of the younger age range. Most of the recorded cases have been just prior to puberty.

We have already pointed out basic differences in the structure of the immature and the mature pelvis. The pelvic floor in the child is relatively thick, muscular, and undifferentiated by the mechanical effects of childbearing. The cul-de-sac is not clearly delineated, and the pelvic organs are small and lack the readily distinguished spatial relationship of the mature pelvis. All of these factors are most important in the examination of the immature pelvis. There are times when the physician trained in pediatric examination may have a definite edge on his confreres. To one especially adept at rectal examination, much may be learned. Tenderness, accompanying pelvic peritonitis, may be more or less localized by careful rectal examination. Rectal examination is almost without pain, even in the young infant. It must be admitted, of course, that vaginal examination is more accurate. In a small child, rough-shod vaginal examination by a large examining finger may do a great deal of harm and is to be condemned as a general practice. It is extremely doubtful if much knowledge can be gained by vaginal manipulations in the infant in any case. In the older child, where possibility of pelvic involvement following gonorrheal vaginitis is really a serious consideration, vaginal examination may be really helpful. Here again, the pediatrician who knows his patient and her parents may be of great assistance. If we know that the emotional background of the patient and the parents is quite stable, vaginal examination may be attempted without much real pain and with little psychic trauma. If, on the other hand, past experience has pointed to a lack of fundamental understanding and stability, the slightest attempt may yield chaotic results. If there is the slightest doubt that the examination will not be successful, it may be wise to use a little gas anesthesia. This should be given to the point of relaxation, and information regarding the tubes and the lower pelvic cavity may be obtained. If past experience with the patient indicates that she reacts favorably to some rapidly acting barbiturate, such as seconal, this can be given. This may make some children quite wild and unmanageable, so the case should be selected. As we know, abdominal palpation may yield considerable information. Time spent in quieting the anxiety of the child and a warm examining hand may localize tenderness, detect muscle spasm, or outline a tumor mass.

In considering the pathogenesis of primary pelvic peritonitis via the ascending route, we have stressed certain anatomic features. The immature pelvis lacks the intricate differentiation of uterus, tubes, ovaries, and broad ligaments. These develop rather rapidly over a short period just prior to and during puberty. The uterus is small, the endometrial glands are mere truncated pits. The tubes are tiny, with a very small lumen and a simple mucosa. The ovaries remain small, and since there are few or no ruptured follicles or corpora hemorrhagica, they are poor soil for infection. Even the young pelvic peritoneum is quite resistant to infection.

Salpingitis, particularly pyosalpinx and hydrosalpinx, is almost never noted in the younger child for the reasons above outlined. In the older girl, the pattern of salpingitis is similar to the adult, except that the infection is apt to localize

higher in the pelvis. Cul-de-sac fluctuation is rare, due to the relatively thick pelvic floor and to lack of structural differentiation.

In diagnosis, there is little to distinguish gonorrheal pelvic peritonitis from other lower abdominal affections. The history is of primary importance. If the child has a vaginal discharge, past or present, which has been gonorrheal, the diagnosis certainly should be suspected. However, we must bear in mind that a child may have gonorrheal vaginitis and suddenly develop acute appendicitis quite independent of the vaginal pathology. Pneumococcus pneumonia of recent date, accompanied by lower abdominal pain is, suggestive. It has been shown that the pneumococcus may occur in the vagina at the same time as it is recovered from the pelvic adnexa, so that we must conclude that an ascending infection is possible here also. One must also consider the possibility of infection from foreign body or rape as a possible factor in pelvic peritoneal involvement. Here, again, a careful history is important.

Temperature and white blood counts are elevated above the level expected in adults, of course. The lack of differentiation of pelvic structures makes the sedimentation rate less reliable than it is in the adult. It must be remembered that there is less tendency to localization and to abscess formation in the child.

The chief importance in differential diagnosis is to distinguish between a primary peritonitis of pelvic origin and a secondary peritonitis from a ruptured appendix, Meckel's diverticulum, or other extension from the gastrointestinal tract. If definite proof of gonococcus or pneumococcus peritonitis can be established, the treatment is conservative. A large initial dose of sulfathiazole by mouth or of sodium sulfathiazole intravenously should be given in a 1 to 5 per cent solution, giving about 1 gr. per pound in the first twenty-four hours. If, on the other hand, one is not reasonably certain of the diagnosis, and there is a possibility of secondary peritonitis, especially from ruptured appendix, surgery should be resorted to and proper drainage established.

In appendicitis, there is more tendency to vomiting and more abdominal pain. This pain may or may not be localized, but right lower abdominal pain is suggestive. The temperature is generally not as high, nor is the white blood count. Sometimes, localization can be detected by rectal examination, when it cannot be by abdominal examination. History of previous attacks is helpful.

In pyelitis, the urinary picture is of utmost importance. Tenderness over the kidney areas may be present. The temperature range is usually higher.

In mesenteric adenitis, history of upper respiratory infection, together with milder course and less localization, is usually present.

Occasionally acute enteritis may be present. The appearances and culture of the stool should make this diagnosis. Not infrequently simple constipation may present a confusing picture. There may be abdominal pain, vomiting, and a low-grade temperature. Again, rectal examination will reveal the cause, and relieve much anxiety.

Primary pelvic peritonitis may, and probably generally does, occur from hematogenous origin. History of upper respiratory infection, or more often of pneumococcus pneumonia, with generalized abdominal pain is suggestive. The age range is considerably younger than with acute appendicitis, the temperature is higher, and the situation is generally more grave. A positive blood culture may be of help. The mortality rate in these cases is high, but is being constantly improved with the use of the sulfonamides.

To return to gonorrheal pelvic peritonitis, which is really our concern here, the condition is rare, but does occur. It is very possible that some cases have gone undiagnosed, and cured. This seems reasonable in view of the small likelihood of tubal involvement. In the rare case where tubal infection does occur, the surgeon may be hard pressed to know whether to remove the tube or not. I cannot attempt to answer this question. There is no doubt in my mind, however, that, if we

recognize vaginal infection early, and start adequate treatment, as previously outlined, there will be less and less of pelvic involvement. With the gradual infiltration of the knowledge to the general public that gonorrheal infection in girls no longer carries a stigma and that cures are relatively simple, we shall have the opportunity to see the cases earlier and the entire problem will be simplified.

In conclusion, let me emphasize the fact that we pediatricians have a responsibility in the treatment of infections of the immature genital tract. With the simplification of this treatment by the use of the sulfonamides, there is no adequate reason why we cannot treat and cure the vast majority of these cases. If cure is not achieved in the relatively short period of two weeks, consultation with a gynecologist can be arranged and little time will have been lost.

DISCUSSION

QUESTION.—Dr. Allen, do you believe that a routine pelvic and vaginal examination of the young teen-age girl is free from emotional shock of severe degree?

DR. ALLEN.—I am sure there is emotional shock of severe degree associated with pelvic examination, not only in the adolescent girl but also in the woman of 42. I see them in the office every day. That is why I wrote this paper in an attempt to change our present training and avoid this emotional shock.

An unmarried woman of 42 came into the office for examination and the emotional shock, connected with giving her history alone, caused the onset of profuse bleeding. The bleeding was so profuse that packing had to be resorted to before she could leave the office. I believe this emotional shock is due to our training or rather lack of training, because the baby and the little girl have none of these reactions. They are quite unconscious of the difference in the different regions of the body. Repeatedly we have to examine 18- or 19-year-old girls, using the deepest type of anesthesia because of the strong reflexes of protection that have been developed in them. They will close their thighs and protect their genitals with their hands and remain rigid under almost any form of the usual anesthesia.

I should like to cite an instance in the St. Louis meeting of the International Congress of Obstetrics and Gynecology which I think is a graphic illustration of what I mean. When we finished our round table discussion on this phase of the gynecologic problems of adolescent children, and questions were called for, none were asked. Finally, in desperation, I said I had hoped that in St. Louis, if not in Chicago, there would be one doctor who did not have this father-daughter complex and might be able to discuss unreservedly the gynecologic problems connected with the pelvic organs of the adolescent child. Following this everyone seemed to want to discuss the general proposition. The first discussant was a woman doctor. "I am glad you said that in just that way. I am 42 and three months ago I went to a prominent Chicago gynecologist for a physical examination. He felt that I was becoming neurotic, and since I had no symptoms, he did not examine my pelvis but suggested that I return only if I had symptoms."

I believe that we should train doctors to examine patients routinely, even in the absence of symptoms, and that we should condition children very early to accept pelvic examination as a routine part of any physical examination. I do not believe that every time a little girl comes to your office she should have a vaginal examination; however, she should be examined thoroughly and progressively so that at the proper time a vaginal examination will not come as an emotional shock but that this region of her anatomy will become a part of her body as a whole.

DR. ASHLEY.—Dr. Sevringhaus brought up the question of the possible danger from overuse of the sulfonamides. That is, of course, a real danger. However, I think we will all admit that sulfonamides are relatively less toxic in children.

In the dosages that are recommended for the treatment of gonorrhea vaginitis, that is, small doses over a period of from ten days to two weeks, very little harm can come. I still feel that at least for us that is the method of choice. There are a couple of questions here in regard to the treatment of chronic nonspecific vaginitis.

One factor must be borne in mind, that with our improved methods of culture technique a great many of these nonspecific cases are actually cases of gonorrhea and more careful diagnostic measures may bring that out. If we cannot culture the gonococcus, we can at least use some method of estrogenic and sulfonamide therapy as outlined for specific cases. In the vast majority of situations that will effect cure.

QUESTION.—What importance do you attach to the wrong use of toilet paper, and secondly, to the habit of many mothers and especially of maids, of washing the vagina with washrag, as causes of vaginitis?

DR. ASHLEY.—In that situation it can be stated that the colon bacillus is a possible cause of pathologic findings in the vagina.

News and Notes

The following have been certified by **The American Board of Pediatrics** following examination in New York City, Nov. 20 and 21, 1943:

Dr. John A. Askin, 2206 Park Ave., Baltimore, Md.
Dr. Leo S. Bell, 37 S. Walnut St., East Orange, N. J. (Now in Army)
Dr. Daniel Blitz, 1 Club Drive, Woodmere, N. Y.
Dr. Joseph Caplan, 103-23 Lefferts Blvd., Richmond Hill, Queens, N. Y.
Dr. Caroline A. Chandler, Children's Bureau, U. S. Dept. of Labor, Washington, D. C.
Dr. Samuel L. Cohen, 674 Linden Blvd., Brooklyn, N. Y.
Dr. Ira H. Degenhardt, 51 Livingston Ave., New Brunswick, N. J. (Now in Army)
Dr. David Dragutsky, 1466 49th St., Brooklyn, N. Y.
Dr. Max D. Garber, Strong Memorial Hospital, Rochester, N. Y.
Dr. Theodore M. Ginsburg, 6056 Spruce St., Philadelphia, Pa.
Dr. Louis Edward Goldberg, 31 Lincoln Park, Newark, N. J.
Dr. Wilson Lyon Grubb, 1011 N. Charles St., Baltimore, Md.
Dr. A. Gerald Heller, 172-20 Northern Blvd., Flushing, N. Y.
Dr. Thomas Franklin Henley, 525 E. 68th St., New York, N. Y.
Dr. Abraham H. Kantrow, 12-26 31st Ave., Astoria, L. I., N. Y.
Dr. Herman Frederick Kotzen, 230 N. 5th St., Reading, Pa.
Dr. Ramon Fernandez Marchante, 234 Ponce de Leon St., Santurce, P. R.
Dr. Rafael R. Muniz, 740 West End Ave., New York, N. Y.
Dr. Martha A. O'Malley, 165 Capitol Ave., Hartford, Conn.
Dr. Louis Platt, Masonic Temple Bldg., Gouverneur, N. Y.
Dr. Edward Press, State Health Dept., Charleston, W. Va. (Now in Army)
Dr. Martha Katherine Reese, 525 E. 68th St., New York, N. Y.
Dr. Benjamin Sachs, Acadia Parish Health Unit, Crowley, La.
Dr. Alex Eugene Schefrin, 235 Lexington Avenue, Passaic, N. J.
Dr. Mollie S. Schildkrout, 69-10 Yellowstone Blvd., Forest Hills, N. Y.
Dr. Herman Schneck, 40 E. 10th St., New York, N. Y. (Now in Army)
Dr. Joseph Frankle Siegel, Boston City Hospital, Boston, Mass.
Dr. Irving Silverman, formerly Boston, Mass. (Now in Army)
Dr. Samuel J. Werlin, 118 Second St., Troy, N. Y.
Dr. Dorothy Hutchinson Welker, 4753 Broadway, Chicago, Ill.
Dr. Arnold Widerman, 430 Pine St., Philadelphia, Pa. (Now in Army)
Dr. Gustav Wilens, 40 Main St., Torrington, Conn.

The following were certified following examination in Cincinnati, Dec. 10 and 11, 1943:

Dr. Charles E. Anderson, Jr., 1560 Line Ave., Shreveport, La. (Now in Army)
Dr. John C. S. Battley, 516 Water St., Port Huron, Mich.
Dr. A. Robert Bauer, 5696 W. Vernor Highway, Detroit, Mich
Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis, Minn.
Dr. Warren F. Belknap, 3666 3-Mile Drive, Detroit, Mich. (Now in Army)
Dr. Stephen C. Bradley, 221 S. 6th St., Terre Haute, Ind.
Dr. Earl W. Brubaker, 1406 Bank of Lansing Bldg., Lansing, Mich.
Dr. Charles Henry Classen, Cushman Road, Rosemont, Pa.

Dr. Karl J. Deissler, 894 Longridge Rd., Oakland, Calif.
Dr. Maurice Bennett Furlong, 14 E. 5th St., Jamestown, N. Y. (Now in Army)
Dr. John Paul Gibson, 202 Grape St., Abilene, Texas.
Dr. Ina Morriss Harper, 611 Fidelity Bldg., Benton Harbor, Mich.
Dr. Willard Z. Kerman, 2039 E. 70th St., Chicago, Ill. (Now in Army)
Dr. Harry Leichenger, 4753 Broadway, Chicago, Ill.
Dr. Lawrence Robert Leviton, Riegel Community Hospital, Trion, Ga.
Dr. Robert R. Macdonald, 448 Brownsville Rd., Pittsburgh, Pa.
Dr. Frank L. Menehan, 912 Brown Bldg., Wichita, Kan.
Dr. Hugo Neuhaus, 131 South Ocean Ave., Freeport, N. Y.
Dr. Frank Church O'Neil, 201 S. Main St., Middletown, Ohio
Dr. Roy Pollack, 48 Henry Ave., Palisades Park, N. J. (Now in Army)
Dr. Saul J. Robinson, 621 16th Ave., San Francisco, Calif. (Now in Army)
Dr. John O. Rydeen, 708 Wainwright Bldg., Norfolk, Va.
Dr. John Richard Schroder, 114 Laurie St., Duluth, Minn. (Now in Army)
Dr. Samuel Spector, University Hospital, Ann Arbor, Mich.

Notice

The American Board of Pediatrics, wishing to take cognizance of the present nature of wartime opportunities for young physicians seeking hospital experience, has ruled that three nine-month periods of graduate training shall constitute acceptable training instead of the previous requirement of three full years of training. Two of the nine-month periods must be spent in a pediatric center, or for a part of the period, not to exceed six months, in a recognized hospital for the care of contagious disease. This ruling may be applied only in those instances where the shorter periods of training were the direct result of the present wartime hospital programs for interns and residents.

In issuing the foregoing ruling the Board is forced to point out that the pressure of emergency conditions can in no way be allowed to lower the standards of its examination. It is contemplated that many candidates will find it necessary to seek additional postgraduate training after the war in order to be prepared properly for the examination.

Book Reviews

The Physiological Basis of Medical Practice. Charles Herbert Best, M.A., M.D., D.Sc. (Lond.), F.R.S., F.R.C.P. (Can.), and Norman Burke Taylor, M.D., F.R.S. (Can.), F.R.C.S. (Edin.), F.R.C.P. (Can.), M.R.C.S. (Eng.), L.R.C.P. (Lond.), ed. 3, Baltimore, 1943, Williams & Wilkins Co., 1,942 pages. Price, $10.

Extensive alterations, additions, and deletions have been made throughout in an attempt to bring the book up to date. The second edition was only four years old, so the appearance of this edition so shortly indicates the rapid changes and the desire to keep the book abreast of current knowledge. Special attention is directed to the section headed "Intracellular Respiration, Respiratory Enzymes, and Energy Liberation," which has been entirely rewritten.

Written primarily for the clinician who must go back to basic physiology constantly to explain the many phenomena observed in his patients. The book fulfills this need admirably and should be within the reach of every physician, especially in the clinical practice of medicine.

McCULLOCH

Source Book of Medical History. Logan Clendening, M.D., New York, 1942, Paul B. Hoeber, Inc., 685 pages. Price, $10.

An anthology of many and varied contributions in the field of medicine given as a comprehensive survey in chronological order. The choice of selections has been made by the author to represent the ideas of each period. Some selections have been made from the lay literature to show a contemporary view of medical life at different ages. Only a few of the selections give the original in its entirety.

A brief chapter of pediatric subjects includes Paulus Bagellardus' *The Little Book of Diseases of Children;* Nicholas Rosen von Rosenstein's *The Diseases of Children and Their Remedies;* Francis Glisson's *De Rachitide;* William Cadogan's *On Nursing and the Management of Children;* and Eduard Heinrich Henoch's *Lectures on Diseases of Children.* An introductory paragraph of this chapter gives references to both Still's and Ruhräh's books on the history of pediatrics with a brief discussion of the very early books in this field. Thus this short chapter could be considered comprehensive of the history of pediatrics, for, in fact, pediatric history shares in other collateral subjects and, of course, has its roots firmly in the past of all the basic and clinical sciences. It should be obvious that pediatrics is not a modern branch of medicine nor an outgrowth of internal medicine but that it has held a place separate and distinct through the centuries. Even William Cadogan's treatise on the care and feeding of infants is really exactly two centuries old. The chapter on Thomas Sydenham includes the discussion of measles, scarlet fever, and the classic description of chorea, to which very little has been added since. Many other chapters also are interesting and pertinent.

The book is not illustrated but is well printed and arranged. For its purpose, it is well suited and is useful as a source of reference and should help create an interest in the history of medicine. It also is pleasant and refreshing to pick up to read at leisure moments. It would do well for some of our present-day reformers to look back into the past occasionally to learn how really modern they might be.

McCULLOCH

Useful Drugs. Edited by Robert A. Hatcher, Phar.M., Sc.D., M.D., and Paul C. Barton, M.D., ed. 13, Chicago, 1942, The American Medical Association Press, 306 pages. Price, $1.

Designed to supply the demand for a selected materia medica and to serve as a basis for both instruction and state board examination in materia medica and therapeutics.

With successive presentations of new editions of this book, it became apparent that it was advisable not only to omit certain pharmacopeial items, but to include certain established preparations which have been declared acceptable for inclusion in *New and Nonofficial Remedies by the Council on Pharmacy and Chemistry.* An indispensable companion for every doctor. It would be a rare occasion which would call for a drug which is not included in this small book. To be used with the new edition of *Epitome of the Pharmacopeia.*

McCULLOCH

La Meningitis Tuberculosa en el Niño. J. Bonaba, A. Carrau, C. Pelfort, and B. D. Correa, Montevideo, 1943, J. Garcia Morales, 175 pages.

This little monograph written by four distinguished Latin-American colleagues is based on the clinical study and observations of over a thousand cases treated in the children's hospitals of Montevideo, Uruguay, during the period from 1908 to 1939. All phases of the subject which are concerned with the etiology, the diagnosis, and treatment of the condition and the pathological anatomy are exhaustively discussed and critically reviewed.

This minute, critical analysis of the subject in conjunction with the illustrative case material is one of the unique values of this monograph.

Tuberculous meningitis is probably the most malignant and hopelessly fatal disease of infancy. This fact has been a discouraging feature in the past as far as scientific investigation in this field was concerned.

The authors point out that this attitude has changed today and there are, on the basis of newer investigation, newer original conceptions regarding the pathogenesis, etiology, and pathology of the condition and a more hopeful outlook as regards this dread disease. It is in the field of prophylaxis where the most effective attack against its inroads is centered. The authors discuss the possibilities along this line extensively. One of the very valuable features of the monograph is the extensive bibliography quoted.

SCHLUTZ

Deshidratacion en Pediatria. Mario J. del Carril y Alfredo E. Larguia, Buenos Aires, 1943, El Ateneo, 351 pages.

This extensive monograph is remarkable for the excellence and completeness with which the material is presented.

The great importance of the acid-base equilibrium and its normal maintenance for normal cell and metabolic function is splendidly and clearly developed. The authors stress its particular importance as a pediatric problem.

All the remarkable advances and knowledge which have been gained in this field in the past two decades are minutely and carefully reviewed and related to the clinical picture of dehydration.

The pathological picture of dehydration and all its harmful effects on the vital functions of the organism are exhaustively discussed.

Full credit and complete discussion are given the fine experimental work contributed by many investigators in many countries, but notably our own, in this field which has led to our present clear understanding of the problem and its intelligent treatment. The authors have contributed a considerable amount of original investigative work. The entire subject is presented with great clarity and every phase is illustrated with excellent graphs and charts. The toxicoses of infancy with their accompanying dangerous states of dehydration are dealt with at great length and the great progress which has been made in the treatment of these conditions is pointed out. It has completely changed the picture of morbidity and mortality in this age group.

Significant publications bearing on any aspect of the subject are critically reviewed and discussed.

The material presented in the monograph is divided into three parts.

The first part deals with the normal metabolism of water and the salts and their interchange in the tissues and body fluids and their distribution.

The second part comprises the clinical investigations and concerns particularly the study of dehydration in the various affections of childhood and the effect they have on the body and the pathological picture which results from water and mineral loss.

The third part is concerned with the actual treatment of the state of dehydration based on the newer concepts developed from experimental and clinical investigative work and deals extensively with the use of plasmotherapy, now considered so effective a remedy in the therapy of the condition. It is one of the best treatises on this important subject which has appeared in recent medical literature and is an outstanding accomplishment of Latin-American pediatrics.

SCHLUTZ

La Glomerulonefritis en la Infancia. Dr. Arturo Gaeza Goñi, Santiago de Chile, 1942, Empresa Editora Zig-Zag, 305 pages.

This excellent monograph is based on the careful observation and study by the author over a period of several years of one hundred fifty cases of acute glomerular nephritis and includes also a review of all such patients observed and treated over a period of ten years in the hospitals Roberto del Rio and Manuel Arriaran and the Casa Nacional del Nino.

The majority of the children studied were between the ages of 3 and 12 years and the highest number between the ages of 5 and 7 years.

The thoroughness with which these cases are studied and investigated at the bedside, the laboratory, at autopsy, and in the pathological laboratory is impressive and highly instructive.

All the recent publications bearing on this subject by colleagues of his own country and leading authorities in other countries are critically reviewed. Especial attention is given to experimental work carried out by such investigators as Goldblatt, Bernardo Houssay, Mazugi, Farr, and others.

A considerable amount of valuable original investigation is reported and data of great value added to shed light on this controversial disease condition.

The various theories regarding its possible etiology are carefully discussed and reviewed and compared with opinions held by the author.

The pathological protocols are most thorough and are accompanied by numerous good illustrations of microphotographs.

The beta hemolytic streptococcus was the most common infectious agent found in the reported series of cases and all others reviewed. The frequency was in excess of 85 per cent.

The author points out the frequency of skin infections such as scabies and impetigo as focal points. In his series of cases it was the focus in over 50 per cent of the cases.

The theories regarding the development of hypertension in this condition are fully considered.

The author warmly defends the Ambard coefficient as a useful test of renal function.

Careful periodic testing of renal function is, in his opinion, most necessary and useful in control of the case and the decision as to when bed rest and rigid dietary measures are indicated.

The chapter on treatment is very exhaustive and complete and embodies all the best and most recent ideas on the subject. There is a particularly fine chapter on the surgical treatment of this condition, involving both the removal of foci of infection and the procedure of decapsulation as practiced by the notable Chilean surgeon, Lobo O'Neil.

This little monograph is without doubt the best and most complete treatise on the subject now available in the Spanish-American literature.

SCHLUTZ

The Journal of Pediatrics

CONTENTS FOR FEBRUARY, 1944

Original Communications

The Mechanism of Muscle Spasm in Poliomyelitis. Herman Kabat, M.D., Ph.D., and Miland E. Knapp, M.D., Minneapolis, Minn. 123

Traumatic Cardiac Injury in a Child With Probable Rupture of Interventricular Septum. Edwin D. Bayrd, M.D., and Stanley Gibson, M.D., Chicago, Ill. 138

Late Effects of Severe Asphyxia Neonatorum. Roy A. Darke, M.D., New York, N. Y. 148

The Effect of Vitamin D From Cod-Liver Oil and a Tuna-Liver Oil Upon Serum Phosphatase Concentrations in Rachitic Infants. Donald J. Barnes, M.D., Bertha Munks, and M. Kaucher, Detroit, Mich. 159

Further Observations on the Use of Single Massive Doses of Vitamin D in the Prevention of Rickets. I. J. Wolf, M.D., Paterson, N. J. 167

Comparative Toxicities of Sulfadiazine and Sulfathiazole in Children. James O. Dowrie, M.D., and Mason H. Abramson, M.D., San Francisco, Calif. 176

Advances in the Chemotherapy of Influenzal Meningitis. Marvin L. Blumberg, M.D., Elk Tannenbaum, M.D., and Morris Gleich, M.D., New York, N. Y. 182

Acrodynia in a Thirteen-Year-Old Boy. Katherine Anderson, M.D., Nashville, Tenn. 186

Congenital Leucemia. Frank S. Cross, M.D., Lansing, Mich. 191

Sublingual Granuloma in Infancy (Riga-Fede's Disease). Mason Abramson, M.D., and James O. Dowrie, M.D., San Francisco, Calif. 195

Fried Food for Children? Frank Howard Richardson, M.D., Black Mountain, N. C. 199

A Psychiatric Consultation Service in a Pediatric Outpatient Department. Mabel Huschka, M.D., New York, N. Y. 206

American Academy of Pediatrics

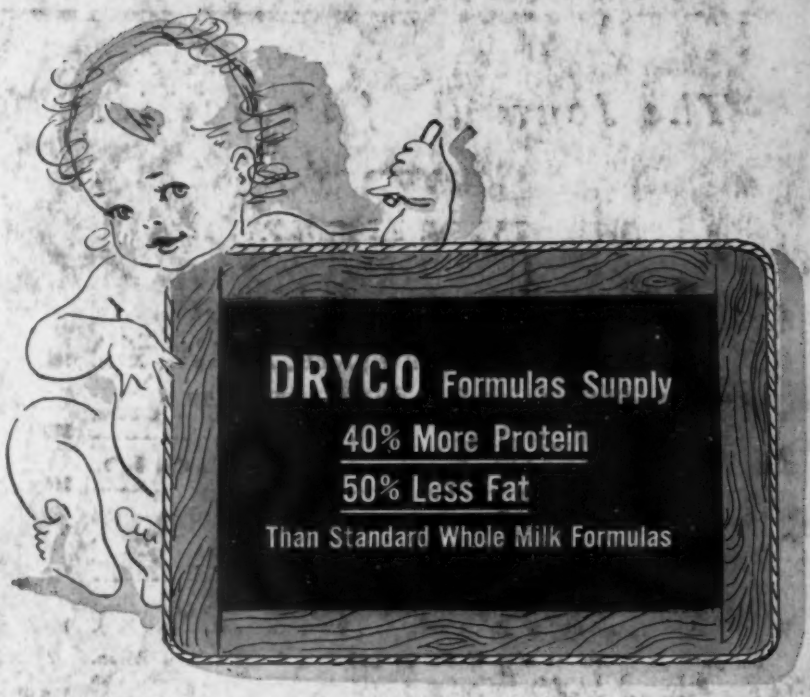
Proceedings: Twelfth Annual Meeting of the American Academy of Pediatrics. Panel Discussion on Pediatric Gynecology 222

News and Notes

News and Notes 244

Book Reviews

Book Reviews 245



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